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Virtual Congress

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european academy of neurology

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Plenary Sessions

Friday, June 18 2021

Congress Opening Session

PLEN01-1

Cerebral organoids: modelling human brain development and neuro-psychiatric disorders in stem cell derived 3D culture

J. Knoblich
Vienna, Austria

The human brain is unique in size and complexity, but also the source of some of the most devastating human diseases. While many of these disorders have been successfully studied in model organisms, recent experiments have emphasized unique features that can not easily be modeled in animals. We use cerebral organoids to recapitulate those features in vitro and to test their role in human disease. Cerebral organoids derived from patients suffering from neuro-developmental disease can recapitulate the developmental defects leading to those diseases and allow us to disentangle the mechanistic complexity of disorders like Epilepsy and Autism. Our new data demonstrate that by studying those defects, we can gain unique insights into the development of the human cortex that cannot be made in rodent model organisms.

Disclosure: Nothing to disclose.

Sunday, 20 June 2021
Presidential Symposium – Named Lectures

PLEN02-1

Moritz Romberg Lecture: Romberg and his famous test – what more do we know 170 years

G. Halmágyi
Sydney, Australia

Romberg, a founder of modern clinical neurology, is now remembered mostly for his postural test in which patients with proprioceptive impairment are unable to stand with their feet together when their eyes shut. Romberg was active before the function of the vestibular system was elucidated and we know that vestibular impairment, moderate bilateral or severe unilateral vestibular impairment will also produce a positive Romberg test, but only if proprioception is disrupted as happens when the patient tries to stand on a compliant rather than on a firm surface. It is now possible to test routinely the function of each of the six semicircular canals and the four otoliths, individually. Here we review the physiological basis of modern vestibular function tests and consider how results from these relate to the Romberg test.

Disclosure: Nothing to disclose.

PLEN02-2

The Brain Prize Lecture

H. Zoghbi
Houston, United States of America

PLEN02-3

Charles Edouard Brown-Sequard Lecture: The core/penumbra model: implications for acute stroke treatment and patient selection in 2021

J-C. Baron
Paris, France

Despite major advances in prevention, ischemic stroke remains among the leading causes of death and disability worldwide. After centuries of nihilism and decades of failed neuroprotection trials, the discovery in non-human primates, subsequently confirmed in humans using positron emission tomography, that after occlusion of the middle-cerebral artery there exists an area of brain tissue termed the ischemic penumbra that is electrically silent and at-risk of infarction, yet can be salvaged by reperfusion up to and perhaps beyond 24 hours after stroke onset, has revolutionized the management of acute stroke patients. Indeed, this discovery underpinned the development of highly efficient reperfusion therapies, first intravenous thrombolysis and more recently endovascular thrombectomy. Importantly, how long the penumbra can survive depends not only on time elapsed since arterial occlusion ('Time is brain'), but also on how severely perfusion is reduced. Imaging techniques allow to map the penumbra and the already irreversibly damaged core in the individual subject, and have documented that the time-course of core growth at the expense of the penumbra widely differs from patient to patient, and hence that individual physiology should be considered in addition to time since stroke onset for decision-making. This concept has been implemented to optimize patient selection using CT or MRI in pivotal trials of reperfusion therapies beyond three hours after stroke onset, and is now routinely applied in clinical practice. The notion that to be both efficient and harmless, treatment should be tailored to each patient's physiological characteristics represents a radical move towards precision medicine for stroke treatment.

Disclosure: Nothing to disclose.

PLEN02-4

Camillo Golgi Lecture: History of prion science

A. Aguzzi
Zurich, Switzerland

Transmissible spongiform encephalopathies (TSEs) are neurodegenerative diseases of humans and many animal species caused by prions. The main constituent of prions is PrPSc, an aggregated moiety of the host-derived membrane glycolipoprotein PrPC. Prions were found to encipher many phenotypic, genetically stable TSE variants. The latter is very surprising, since PrPC is encoded by the host genome and all prion strains share the same amino acid sequence. Here I will review what is known about the infectivity, the neurotoxicity, and the neuroinvasiveness of prions. Also, I will explain why I regard the prion strain question as a fascinating challenge – with implications that go well beyond prion science. Finally, I will report some recent results obtained in my laboratory, which is attempting to address the strain question and some other basic issues of prion biology with a "systems" approach that utilizes organic chemistry, photophysics, proteomics, and mouse transgenesis.

Disclosure: Nothing to disclose.

Monday, June 21 2021
Towards Precision Neurology

PLEN03-1
Epidemiology meets deep learning and artificial intelligence

M. Van der Schaar
Cambridge, United Kingdom

PLEN03-2
Current and future use of precise tools (e.g. genetics, biomarkers, imaging) for personalized

H. Zetterberg
London, United Kingdom

PLEN03-3
Individual treatment decisions based on precision neurology

F. Muntoni
London, United Kingdom

Spinal muscular atrophy is an ideal condition in terms of genetic therapeutic intervention. All patients with SMA, irrespective of their severity, have homozygous deletions (or other mutations) of the SMN1 gene, but carry at least one intact copy of the SMN2 gene. These two genes are virtually identical, with the exception of the splicing regulation of exon seven, excluded from the majority of the transcript in SMN2. This led to the development of compounds to modify SMN2 gene exon seven splicing, which were the first one to be studied across the broad SMA patient population. More recently it has been possible to deliver the SMN1 gene using an AAV viral vector, and the development of this therapeutic intervention has also progressed rapidly. We are now in the unusual situation in which, in the last five years, SMA shifted from an incurable disease, to a condition in which there are now three approved drugs. The pace of changes in the SMA field is unprecedented in neurology and provides a paradigm for therapeutic development also in other neurological conditions. At the same time, the field is facing now new issues: 1. Treatment efficacy is tightly associated with duration of disease, so early recognition and intervention are now more important than in the past; 2. A new "generation" of children who would have had a very severe and eventually fatal disease are now surviving and demonstrating significant improvement, however we are not sure on how their phenotype will evolve over time; 3. As the three drugs are unequivocally effective, high quality comparative analysis of their individual efficacy is currently not available, and of course this leads to some uncertainties on "the best approach" both for families and treating physicians; 4. Is combinatorial therapy a rational step from a medical perspective, apart from the financial considerations? The evolution of this field will be summarised in my presentation

Disclosure: Nothing to disclose.

PLEN03-4
Precision Medicine without limits? Ethical and economic challenges

C. Druml
Vienna, Austria

Symposia

Saturday, June 19 2021
Five Presidents Symposium: Future of Sleep Medicine

SYMP01-1

Sleep Apnea and Cerebrovascular Disease – 2021 update

J. Stevens
Fort Wayne, United States of America

This lecture will discuss current knowledge concerning the complex interaction between sleep, sleep disorders, cerebrovascular disease and stroke, with a particular emphasis on sleep apnea. Recommendations concerning primary and secondary prevention of stroke by providing treatment of sleep-related conditions will be provided.
Disclosure: Nothing to disclose.

SYMP01-2

REM Sleep Behaviour Disorder (RBD): future implications for neurodegenerative disease

C. Trenkwalder
Kassel, Germany

Idiopathic or isolated REM sleep behavior disorder (iRBD) is defined by the International Classification of Sleep Disorders (ICSD-3, Sleep 2014) and includes a pathologically increased muscle tone of the chin (REM without atonia, RWA) (Frauscher et al Sleep 2012) during the REM episodes recorded by video-polysomnography (PSG). REM episodes are clinically characterized by vocalizations, jerky movements, even bed falls or violations of the patient or the bedpartner. As questionnaires are not sufficiently valid for diagnosis, video-synchronized PSG is the gold standard for diagnosis. Currently, iRBD is the most specific prodromal feature of α-synuclein pathology, which may manifest even a decade before motor symptoms of Parkinson disease, multiple system atrophy or dementia with Lewy Bodies occur. In a 18-year follow-up study more than 80% of the subjects of a cohort with iRBD have developed a neurodegenerative disease (Schenck et al, 2013). Recent data report an overall conversion rate from iRBD to an overt neurodegenerative syndrome of 6.3% per year, with 73.5% converting after 12-year follow-up (Postuma et al 2020). The prevalence of RBD in de novo PD patients is about 25% (Mollenhauer et al 2013), with an increase up to 52% in the same cohort after six years (Zimansky et al 2021). RBD is now established as a diagnostic marker for DLB and occurs up to 80% in patients with MSA. The early diagnosis of RBD combined with other non-motor features such as hyposmia, constipation, depression and cognitive decline characterizes the prodromal phase of a neurodegenerative syndrome, most likely a alpha-synucleinopathy. Unfortunately none of these non-motor parameters and RBD can be shown in each single PD patient, some PD patients even miss many of these non-motor features or develop them later in the disease. The early diagnosis of iRBD, however, provides an unprecedented opportunity to directly observe prodromal neurodegenerative states, for early intervention with neuroprotective therapy, if available in the future.
Disclosure: Nothing to disclose.

SYMP01-3

Narcolepsy: An immune-mediated hyothalamic disease

C. Bassetti
Bern, Switzerland

Narcolepsy affects one of 2,000 people in the general population and typically starts in adolescence and early adult life. The leading symptom is excessive daytime sleepiness (EDS) with (narcolepsy type 1, NT1) or without (NT2) cataplexy. Other manifestations include hallucinations, sleep paralysis, disturbed sleep, as well as cognitive, psychiatric, metabolic and autonomic disturbances. The etio-pathophysiology consists of genetic and environmental factors which lead to an immune-mediated loss of orexin neurons in the lateral hypothalamus. Rarely, narcolepsy is seen in the context of other acquired or familial brain diseases. Diagnosis is based on clinical features and supported by the presence of typical biomarkers (sleep onset REM episodes, cerebrospinal fluid orexin deficiency, HLA DQB1*06:02 positivity). Current diagnostic criteria for NT2 and the narcolepsy borderland are controversial. Symptomatic treatments for EDS, cataplexy and other symptoms have greatly improved, their evidence and efficacy were recently reviewed (EAN-ESRS-EU-NN guidelines, 2021). More research is needed to determine the exact frequency of narcolepsy, identify new biomarkers, uncover the exact mechanisms of orexin loss, and determine the potential of new (also causal) treatment approaches and their impact on patients' functionality and quality of life.
Disclosure: Nothing to disclose.

SYMP01-4

Restless Legs Syndrome: Recent results from pathophysiological and imaging studies.

B. Högl
Innsbruck, Austria

SYMP01-5

Is Paradoxical (REM) sleep a motor state?

P.-H. Luppi
Lyon, France

EAN/MDS-ES Updates in Innovative Diagnostic Methods for Parkinson's disease and other Synucleinopathies

SYMP02-1

Imaging for Parkinson's disease and Parkinsonism

I. Rektorova
Brno, Czech Republic

SYMP02-2

Has Genetics Changed Management of Parkinson's disease and other Synclinopathies

A. Di Fonzo
Milan, Italy

In recent years, the identification of various genetic causes of Parkinson's diseases and other Synucleopathies has had a great impact on a better definition of different clinical syndromes. The advent of next-generation sequencing techniques has provided an impressive step forward in the easy identification of PD monogenic forms. However, this increased availability of genetic testing has challenges, including the ethical issue of genetic testing in unaffected family members, available home testing kits and the increasing number and relevance of variants of unknown significance. The emergent role of genetic factors in PD has important implications on clinical practice and counseling. As a consequence, it is fundamental that neurologists have a proper knowledge of the genetic background of this disease and perform an accurate selection of when and who has to be tested for gene mutations.
Disclosure: Nothing to disclose.

SYMP02-3

Laboratory biomarkers for diagnosis of PD, other synucleinopaties and atypical parkinsonian syndromes – is there evidence?

P. Svenningsson
Stockholm Sweden

The degeneration of dopaminergic neurons of the midbrain together with the deposition of intracytoplasmic aggregates of alpha synuclein (α-syn) constitute the main pathological hallmarks of Parkinson's disease (PD) and Multiple System Atrophy (MSA). The search for a reliable diagnostic and prognostic biomarker in PD has seen increased attention towards the exploration of measures of α-syn species of peripheral tissues and biofluids. Autopsy studies of PD patients have confirmed the frequent co-existence of α-syn pathology in the brain and the peripheral nervous system (PNS) and cerebrospinal fluid (CSF). In this presentation, I review research mainly from the recent years investigating the biomarker potential of detecting peripheral α-syn pathology with regard to feasibility, methodology and diagnostic accuracy. We reference studies using different methodologies, from well-established immuno-histochemistry (ICH) to novel proximity ligation assay (PLA) assays seeding propensity using Real-Time Quaking-induced Conversion Studies (RT-QuIC). I also discuss studies measuring α-syn in extracellular CSF vesicles. In addition, studies on neurofilament light chain (NfL) in CSF as well as serum/plasma show a high specificity to distinguish PD from MSA as well as the taoupathies progressive supranuclear palsy (PSP) and corticobasal syndrome (CBS).
Disclosure: Honorarium from AbbVie

SYMP02-4

Neuropathologic Signature of synuclein dissemination in Parkinson's disease

T. Outeiro
Gottingen, Germany

Parkinson's disease (PD) is a progressive, age-associated neurodegenerative disorder affecting more than 10 million people above 60 years old. Neuropathologically, PD is characterized by the accumulation of aggregated protein deposits known as Lewy bodies and Lewy neurites, primarily composed of alpha-synuclein (aSyn). aSyn is an abundant brain protein involved in synaptic vesicle release, and is known as an intrinsically disordered proteins (IDP) with prion-like properties, as it can misfold, seed, and spread the misfolded conformation to normal monomeric forms of the protein. Different strains of aSyn and seem to display different cell binding and penetration properties, resulting in the transmission of pathology between cells. It is currently thought that distinct protein conformations account for differences in seeding potency. Interestingly, different studies reveal the occurrence of multiple types of protein pathologies in PD and other neurodegenerative disorders, suggesting a putative synergistic effect in the aging brain that may culminate in multi-morbidity. However, the exact molecular mechanisms involved in the cross-talk between different proteins, and in the propagation of aSyn pathology, are still obscure. Here, I will discuss current concepts suggesting the pathological spreading of aSyn aggregation in PD.
Disclosure: Nothing to disclose.

EAN/ILAE Post-stroke epilepsy – on the way to precision neurology

SYMP03-1

Epileptogenesis after intial insult

A. Pitkänen
Kuopio, Finland

More than five million people are diagnosed with epilepsy every year. Despite of about 30 anti-seizure drugs, 30% of patients are drug-resistant. The International League Against Epilepsy has recently proposed a classification of epilepsies into six etiologic categories: structural, genetic, infections, metabolic, immunological, and unknown. Preclinical and clinical molecular, cellular, and network research have shown etiology-dependent differences in the progression of epileptogenesis (i.e., development of epilepsy and its progression). Preclinical studies have demonstrated promising anti-epileptogenic or disease-modifying effects in structural and genetic etiologies with more than 50 interventions, ranging from small molecules, to biologicals, to cell and gene therapies. Several molecular, imaging, and electrophysiologic parameters have shown promise as prognostic biomarkers for epileptogenesis. However, major efforts will be required to validate and translate the promising proof-of-concept data to clinical practice in order to reduce the incidence of epilepsy or at least reduce the molecular tissue pathology to the level, at which the epilepsy stays drug-responsive. Data points towards precision treatment(s) that match with etiology, molecular pathology of epileptogenesis and subject-specific genetic and exposomal factors.

Disclosure: NeuroTrauma Sciences, Corlieve Therapeutics, Angelini Pharma - consultations fees.

SYMP03-2

Stroke, Seizures, and Epilepsy – Precision from the clinical perspective

T. Von Oertzen
Linz, Austria

Prevalence in epilepsy, whilst high in the first two decades of life, tend to peak in the elderly. Cerebrovascular disease is the most common cause of epilepsy in adulthood. Seizure after stroke may occur early (within seven days of acute stroke) or late (after seven days of acute stroke). Whereas early seizures tend to reflect impact of acute changes, late seizures are more likely to present epilepsy. Although post stroke seizure and epilepsy seem to affect only a minority of stroke patients, recent studies identified risk factors for post stroke epilepsy. Hence, identification of patients with particular risk profile is feasible. The number of anti-seizures medications (ASM) has dramatically increased since the early `90th, little data exist on the effect of specific ASMs in the elderly or stroke. Most data show better tolerability of third generation ASM but no difference in seizure control.

Inflammatory effects are discussed to contribute to post stroke epileptogenesis. However, data on anti-inflammatory aspects of e.g. statins or on post stroke epilepsy are sparse. Seizure prediction scores including SeLECT score for ischemic strokes and CAVE for intracerebral hemorrhage allow stratification of high risk groups. This will allow meaningful clinical trials on post stroke epilepsy which will ideally lead to more precise treatment option for epilepsy or even neuroprotection to prevent post stroke epileptogenesis.

Disclosure: Dr. von Oertzen reports grants, personal fees and/or non-financial support from Novartis Pharma, Eisai, UCB, Arielle, GW Pharma and Livanova.

SYMP03-3

Infections as etiology of epilepsy, treatment and prognosis

M. Koepp
London, United Kingdom

SYMP03-4

Post-traumatic epilepsy – current treatment

M.H. Bjørk
Bergen, Norway

Post-traumatic epilepsy is defined as seizures occurring more than seven days after traumatic brain injury. Seizures occurring within seven days of injury are classified as early post-traumatic seizures. Approximately 4% of all epilepsy cases are post-traumatic, and it's the most important cause of symptomatic epilepsy in young people. After traumatic brain injury, the 10-year incidence is 2–4% and increases with injury severity. In severe brain injury, more than 10% of patients develop epilepsy. Other risk factors are early post-traumatic seizures, impressed skull fractures, penetrating brain injuries, intracranial hemorrhage, temporal/frontal cortical damage, chronic alcohol consumption, psychiatric disease, a family history of epilepsy, and repeated head injuries, as well as abusive head trauma in children. Post-traumatic epilepsy may develop several years after the injury, but more than 50% of patients experience their first seizure within the following year. The cascade of events leading to post-traumatic epilepsy include excitotoxicity, neuroinflammation, oxidative stress, and neurodegeneration. Many patients develop hippocampal sclerosis. Anti-seizure medication prevents early post-traumatic seizures and is recommended in high-risk patients to avoid further brain injury and status epilepticus. Meta-analyses have shown that levetiracetam and phenytoin/fosphenytoin are equally effective, but levetiracetam is easier to administer and better tolerated. Anti-seizure prophylaxis does not reduce the risk of post-traumatic epilepsy and should be tapered down after hospital discharge. Several agents have had promising anti-epileptogenic effects in animal studies but have not been tested in humans. Post-traumatic epilepsy is treated with anti-seizure medication recommended for focal epilepsy. Surgery can be considered for select patients.

Disclosure: Bergen Epilepsy Research Group, led by Dr Bjørk, has received funding from Sanofi to conduct post-marketing drug safety research. Speaking/consultancy honoraria from Novartis, Teva and Lilly.

Are we able to prevent some symptoms in neurogenetic disorders?

SYMP04-1

Are we able to prevent or minimize the symptoms in leukodystrophies?

L. Schöls
Tübingen, Germany

SYMP04-2

How early diagnosis helps to prevent the cardiological manifestations in neuromuscular disorders

M. De Visser
Amsterdam, The Netherlands

SYMP04-3

Personalized preventive approaches for stroke prevention in neurogenetic disorders

A. Arsovska
Skopje, Macedonia

Stroke is one of the leading causes of disability and mortality in the world. Despite the advances of treatment modalities, it is still a challenging subject. Stroke is a complex and multifactorial disease caused by the combination of vascular risk factors, environment and genetic factors. Personalized preventive medicine is a relatively new platform that can guide the clinician to create an optimal prevention pathway for stroke in patients with neurogenetic disorders. It is also important to establish an accurate diagnosis through detailed evaluation of such patients. It will also lead to improved risk assessment and family counselling, as well as increased awareness for neurogenetic causes of stroke.
Disclosure: Nothing to disclose.

EAN/EAPC Personalised palliative care for chronic progressive neurological disease

SYMP05-1

Advancing precision care in advanced MS – the EAN Guideline

A. Solari
Milan, Italy

The Clinical Practice Guideline on Palliative Care (PC) of People with Severe Multiple Sclerosis (MS) was a joint initiative of the EAN, EAPC, RIMS, and has been endorsed by ECTRIMS and MSIF. The guideline followed the GRADE methodology, and was devised by a task force of health professionals (HPs) from three disciplines (neurology, PC, and rehabilitation), methodologists, and patient advocates from nine countries. Ten clinical questions were formulated, involving HPs and over 950 MS patients and caregivers from the participating countries. These clinical questions encompassed general and specialist PC, advance care planning (ACP), discussing with HPs the patient's wish to hasten death, symptom management, multidisciplinary rehabilitation, interventions for caregivers (two questions), and interventions for HPs (two questions). For six of the clinical questions (general and specialist PC, symptom management, multidisciplinary rehabilitation, and interventions for caregivers) 34 evidence-based recommendations were produced (one of which was a strong recommendation) and one good-clinical-practice statement. Six additional statements were formulated for the clinical questions where evidence was lacking: ACP, discussion with HPs of the patient's wish to hasten death, and interventions for HPs. Besides providing evidence-based guidance to HPs involved in the care of people with severe MS, this guideline emphasizes the need for further research on the integration of PC and MS care, including consideration of the various models of (palliative) care provision in this population. To help bridge this knowledge gap, selected task force members are now leading a project aimed to constructing and testing the efficacy of a MS-specific ACP intervention.

Disclosure: Dr. Solari reports grants from the EAN and the FISM, during the conduct of the study; other from Almirall, Excemed, Genzyme, Merck Serono, Novartis, and Teva, outside the submitted work.

SYMP05-2

Personalised Care of Late Stage Parkinsonism – the CLaSP study

S. Lorenzl
Salzburg, Austria

SYMP05-3

Personalised palliative care improves quality of life for neurological patients

D. Oliver
Canterburry, United Kingdom

Palliative care has been recommended for the care of people with progressive neurological disease and is now included in many disease specific guidelines. Palliative care encompasses the personalised, holistic care of all patients -physical, psychological/emotional, social and spiritual - and in particular those with life limiting disease. All patients should receive good communication with patient and family, shared decision making and goal setting and symptom management, and this should be available due to their needs, rather than the state of progression of the disease. Specialist palliative care services, from a specialist team, may be needed for complex issues, including complex communication and ethical issues at the end of life. There is increasing evidence that palliative care is effective. A short-term intervention for people with multiple sclerosis (MS) and the training of specialist MS nurses improved symptoms and reduced care giver burden, both of which would reflect on quality of life. A large UK trial of a short-term intervention showed improvement in symptoms – pain, sleep, nausea and bowel issues- with no change in mortality, and patients and families appreciated the care and felt more empowered. A trial of a multidisciplinary specialist palliative care team involvement did show an improvement of quality of life, as well as symptom improvement. The careful, personalised assessment and management by a specialist team, with palliative care and neurological experience, does seem to be effective. Further research is needed in this complex area, to continue to develop this established evidence base.

Disclosure: Nothing to disclose.

EAN/EANO Precision Neuro-oncology

SYMP06-1

Targeted therapy for glioblastoma

E. Le Rhun
Zurich, Switzerland

SYMP06-2

Targeted therapy for rare brain tumors

R. Rudá
Turin, Italy

Rare CNS tumors represent a unique challenge. Given the difficulty of conducting dedicated clinical trials, there is lack of therapies supported by high quality evidence, and knowledge regarding the impact of standard treatments (surgery, radiotherapy or chemotherapy) is commonly based on retrospective studies. Recently, new molecular techniques have led to the discovery of actionable molecular alterations. The aim of this talk is to review the recent progress into molecular understanding and therapeutic options of some rare brain tumours, both in children and adults. We will discuss options such as targeting m-TOR pathway in subependymal giant cells astrocytomas (SEGAs) of tuberous sclerosis and BRAF V600E mutation in rare glial (pleomorphic xanthoastrocytomas) and glioneuronal (gangliogliomas) tumors. These two tumor entities are a model of how specific molecular treatments can favourably impact neurological symptoms, such a seizures or quality of life, and outcome. Moreover, we will discuss the initial experience in targeting new molecular alterations in diffuse gliomas, such as IDH mutations and NTRK fusions, and in medulloblastomas, such as SHH pathway.
Disclosure: Nothing to disclose.

SYMP06-3

Targeted therapy for brain metastasis

M. Preusser
Vienna, Austria

SYMP06-4

Targeted therapies for brain tumors in children

S. Müller
San Francisco, United States of America

Disorders of Spatial Orientation and Navigation

SYMP07-1

Effects of aging and Alzheimer's disease on spatial navigation

V. Segen
Magdeburg, Germany

Normal aging is associated with declines in navigational skills, including path integration, spatial learning, formation of allocentric representations, and spatial memory. The deficits experienced by Alzheimer's disease (AD) patients are even more pronounced and have significant implications for everyday functionality. Spatial navigation deficits observed in AD, including asymptomatic at-risk young adults, are associated with pathological changes within the medial temporal lobe, primarily the entorhinal cortex and the hippocampus. In fact, those areas are the earliest regions that show tau accumulation, a hallmark of AD pathology, as well as to undergo substantial structural and functional changes. Converging evidence suggests that the same regions play a key role in supporting spatial navigation. For example, the entorhinal cortex is a critical region for path integration, whilst the hippocampus is closely linked with landmark-based navigation and spatial memory. In this talk, a review of spatial deficits observed in healthy older adults and AD patients will be provided. Specifically, the talk will focus on age-related changes in spatial memory across different perspectives as well as declines in path integration. Lastly, the potential of assessing path integration performance using virtual reality technology as an early diagnostic tool for those at risk of developing AD will be highlighted.

Disclosure: Nothing to disclose.

SYMP07-2

Spatial navigation deficits as cognitive markers for preclinical Alzheimer's disease

J. Laczo
Prague, Czech Republic

Currently, there is an urgent need to identify individuals with preclinical Alzheimer's disease (AD) who may benefit from potential prevention strategies and disease modifying therapies. Neuroimaging, cerebrospinal fluid and newly also blood-based biomarkers are used as diagnostic measures of AD pathophysiology in the preclinical stage. By contrast, there are no established cognitive markers to identify preclinical AD and at-risk individuals. The brain areas that are highly susceptible to and affected earliest by AD pathophysiology constitute the core network for spatial navigation. Therefore, spatial navigation deficits may reflect underlying AD pathophysiology in the preclinical stage of the disease. In accordance with this theoretical model, recent studies have demonstrated that individuals with preclinical AD and genetically at-risk individuals show altered spatial navigation patterns before any other cognitive symptom onset. Spatial navigation deficit is thus emerging as a potential cost-effective cognitive marker to detect AD in the preclinical stage, which has important implications for future diagnostics and treatment approaches.

Disclosures: Nothing to disclose.

SYMP07-3

Neurological disorders of spatial orientation and navigation

T. Brandt
Munich, Germany

Neurologists become increasingly aware that impairment of spatial orientation, spatial memory and navigation are found in patients with degenerative brain disorders, especially impending dementia, transient global amnesia, acute right hippocampal lesions and in patients with bilateral peripheral vestibular loss. Real-space navigation can differentiate between amyloid-positive and amyloid- negative amnestic mild cognitive impairment and thus identify patients with Alzheimer pathology (Schöberl et al. Neurology 2020). Prolonged allocentric navigation deficits disclosed hippocampal damage in transient global amnesia (Schöberl et al. Neurology 2019). PET measurements in the post-acute stage revealed activations in the right hippocampal and extrahippocampal cerebral navigation network as a functional substitute for the deficit in creating an updating of the internal cognitive map. Transient topographical disorientation may occur with right hippocampal hemorrhage (Irvin et al.Brain Behav 2018). Patients with bilateral vestibulopathy show spatial memory deficits in a virtual variant of the Morris Water Task accompanied by a hippocampal volume loss (Brandt et al. Brain 2005). Spatial navigation requires a continuous representation of the location of motion of the individual within a 3-D environment whose coordinates are provided mainly by vestibular and visual cues. This information is essential for an update of our internal model of the environment and the establishment of actual cognitive maps during locomotion. In real-space experiments selective deficits in recombining novel routes (shortcuts) were found (Schöberl et al. Sci Rep 2021). A chronic unilateral vestibular loss does not significantly affect spatial memory (Hüfner et al. Hippocampus 2007)

Disclosure: Nothing to disclose.

Monday, June 21 2021

The next revolution for neurotherapy? Navigated transcranial ultrasound for surgery, blood brain barrier opening and neuromodulation

SYMP08-1

Focal surgery with ultrasound

A. Lozano
Seville, Spain

The delivery of focused ultrasound energy across the skull represents a novel non-invasive means of making therapeutic lesions in the brain. So far, approximately 2,000 patients per year are receiving focused ultrasound thalamotomy to treat essential tremor and other tremor disorders. These procedures typically take two hours to perform and are often done in an outpatient basis. With the therapeutic success and safety of these procedures the possibility of additional targets and novel pathologies are being considered. There is a possibility of lesioning the globus pallidus and the subthalamic nucleus in addition to the thalamus to treat Parkinson's disease, and a number of neuropsychiatric targets including the anterior limb of the internal capsule and the subgenual cingulate are also being considered to treat disorders such as obsessive-compulsive disorder and depression. In addition, there are a number of emerging indications of focused ultrasound to treat a variety of neurological disorders, which will be discussed.
Disclosure: Nothing to disclose.

SYMP08-2

Focal blood brain barrier opening with ultrasound

J.-F. Aubry
Paris, France

Transcranial ultrasonic brain therapy emerged during the past decade as a new clinical tool for neurology. High power multi-element arrays of transducers have been developed for focal surgery and successfully used for thalamotomy, in particular to treat Essential Tremor, Parkinsonian Tremor, neuropathic pain, or Obsessive Compulsive Disorders. The same clinical systems have been operated at lower power and in conjuction with intravenous injection to ultrasonic contrast agents (micro-bubble) to open the blood brain barrier (BBB). Such transient and local drug delivery in the brain paves the way to more efficient drug therapies, such as chemotherapy for glioblastomas.We will present in this talk the principles of ultrasound-induced BBB opening, and the results of pioneering BBB opening in humans with Magnetic Resonance Guidance. We will also show that lightweight handheld and neuronavigated systems have been developed specifically for BBB opening and are now available. We will finally show how BBB opening can be used to deliver neuroactive drugs to modulate brain activity, bridging the gap with another promising application of transcranial ultrasound: transcranial ultrasound stimulation (TUS).
Disclosure: Nothing to disclose

SYMP08-3

Focal neuromodulation with ultrasound

R. Beisteiner
Vienna, Austria

Models for explaining phenotype(s)

SYMP09-1

Clinical heterogeneity of Neurogenetic diseases: introductory overview

A. Federico
Siena, Italy

The phenotypic variability in rare genetic neurologic disorders is well known to clinicians and neuroscientists. For the same disorders, in fact, we may have a different age onset, on neonatal, on early or late infantile, on juvenile and on adult ages, sometime differently occurring even in the same family. The phenotypic variability may also present with a variable symptomathology of the same disease (related to a dismetabolic condition secondary to a gene abnormality), with mainly psychic changes, or with different involvement of the central (brain cortex, white matter, basal ganglia, cerebellum, medulla) or even of peripheral nervous system and muscle alone. We will report several examples of inherited rare neurologic disorders, describing the different phenotypic presentations, the primary genetic changes and the role of gene mutations that may differently alter the protein metabolism with consequences in clinical presentations, the possible involvement of secondary gene changes which may interact with the primary genetic defects, the role of inflammation processes and finally of exogenous factors as environment, trauma, etc., all factors able to deeply influence the phenotypic presentation.

Disclosure: Nothing to disclose.

SYMP09-2

One gene and variable onset and phenotype

J.M. Burgunder
Guemligen, Switzerland

Different mutations from a single gene may lead to very variable phenotypes, and this is mostly due to the level of perturbation of the encoded protein. Relationship between genotype and phenotype, is a complex and variable phenomenon. Phenotype variations include age at onset, course and presentation. The molecular mechanisms underlying such a variation are being extensively explored and this research has provided a number of answers. They can be classified in those involving the mutation itself and other due to genetic, epigenetic and environmental factors. One of the best explored examples is Huntington's disease, in which the age at onset is often decreasing from one to the next generation due to a dynamic mutation. The role for this mechanism has also been established in other diseases including some of the spinocerebellar ataxia and myotonic dystrophy. In other disorders, differential parental imprinting with variation in methylation accounts for differences in phenotype. Likewise, variations in gene sequences not directly related to the disease may also influence the phenotype. For example, genome-wide studies in large populations of Huntington's disease patients have demonstrated the association of variations in genes related to DNA repair functions with age at motor onset. In some instances, such information is already important in terms of neurogenetic counselling, whilst in other it is still more relevant in terms of patients populations. Furthermore, knowledge about these mechanisms has lead to a better understanding about pathogenetic aspects in a number of neurogenetic disorder, and may eventually provide improved avenues for treatment.

Disclosure: Nothing to disclose.

SYMP09-3

The importance of gene-gene interactions in neurological disorders

J. Molnar
Budapest, Hungary

From simple Mendelian diseases to complex genetic disorders novel methods are developed to diagnose, treat and cure these disorders. In monogenic disorders cc. 31% of disease genes have more than one disease phenotype association (pleiotropy). It means that one gene can interact in complex ways. In other disorders two or more different genes can act together to modify a phenotype with the mechanisms of epistasis. Digenic inheritance is associated with two loci that are required for expression of single Mendelian condition. Oligogenic inheritance is associated with the presence of several rare variants. Mendelian condition pairs can involve one or more modes of inheritance (AD+AD, AD+AR, AR + AR). Mutational burden is observed when the phenotype associated with a highly penetrant variant is modified by the presence of one or more additional variants which by themselves are not penetrant. In common disorders there is an increasing need for disease prediction. Based on the recent observation the polygenic risk scores are the best predictors. Whether and how subthreshold risk loci translate into relevant disease pathways is unknown. The lecture will emphasize the importance of the gene-gene interactions in both rare and common neurological disorders. The challenges of the genetic counselling with complex inheritance will be discussed. Finally, you will get an insight into the newest results of the polygenic risk score research in common neurological disorders.

Disclosure: Nothing to disclose.

SYMP09-4

Gene-environments interactions

L. Migliore
Pisa, Italy

Chrononeurology – rhythmicity in neurological disorders

SYMP10-1

The Biological Clock and Neurological Diseases

D. Skene
Surrey, United Kingdom

SYMP10-2

Rhythmicity in Headache Disorders

C. Schankin
Bern, Switzerland

Primary headache disorders, such as migraine, cluster headache and other trigeminal autonomic cephalalgias, hypnic headache and others, are characterized by a predisposition to headache attacks of a specific phenotype. That means that the presence of a combination of several internal and external factors may trigger headaches in patients with a certain genetic background. Over recent years, the mechanisms of these factors have been investigated in detail using clinical presentation, genetics, neuroimaging and animal work. Most of the primary headache disorders are subject to a striking internal rhythmicity that might either modulate the predisposition to attacks, as seen for example in cluster headache patients in bout compared to out of bout, or the triggering of attacks itself. Deciphering the mechanisms of headache chronobiology will improve our understanding of the pathophysiology of attack generation, and it might reveal novel approaches for prophylactic treatment. In this presentation, the focus will be on our current understanding of the rhythm generators of different primary headache disorders. We will discuss if and how they can be modified, and what could be potential treatment options in the future.
Disclosure: Consulting, Advisory Boards, Speaker, Travel Support for/from Novartis, Eli Lilly, TEVA Pharmaceuticals, Allergan, Almirall, Amgen, MindMed, Grünenthal. Part-time employee at Zynnon.

SYMP10-3

The Timing of Stroke

S. Evers
Münster, Germany

The timing of stroke onset is dependent from many variables including biorhythmicity. In this presentation, the different aspects of these variables will be presented. This includes the 24 hour-rhythm which is mainly influenced by endocrinological and homoeostatic factors sich as stress hormone levels, blood pressure, temperature etc. Also differences in the occurrence of stroke can be detected during a week. Here, more social aspects have to be considered. Finally, also the annual biorhythm has been detected to have some impact on the occurrence of stroke. Weather changes and environmental factors are important in this context. In summary, stroke medicine is also influenced by different rhythmic levels on a daily, weekly and annual basis.
Disclosure: Honoraria received from Allergan, Lilly, Novartis, Teva

SYMP10-4

How sleep and sleep loss affect brain disorders

R. Fronczek
Leiden, The Netherlands

This lecture will highlight the role of sleep in relationship with the biological clock in neurological disorders. The newly discovered glymphatic pathway plays a vital role in clearing amyloid from the brain during sleep. In alpha-synucleinopathy's and paraneoplastic disorders sleep symptoms are an early core feature, offering possibilities for early diagnose and possible disease course modifying interventions.
Disclosure: Lecture fees & Advisory Work: TEVA, Novartis, Bioprojet, Allergan, Lilly.

Tuesday, June 22 2021
EAN/ESO Recent advances in acute stroke pathophysiology and treatment

SYMP11-1

Covert Brain Infarction: Towards Precision Medicine in Research, Diagnosis, and Therapy for a Silent Pandemic

T. Meinel
Bern, Switzerland

Covert brain infarction (CBI) is by far the most frequent incidental finding on brain imaging outweighing all other incidental findings on brain imaging combined. It is estimated, that CBI are up to three times more prevalent then manifest stroke. The aim of this talk is to present the current evidence on the history, neuroradiological definitions, pathophysiology and consequences of CBI. One particularly relevant question for neurologists is whether a standardized or individualized diagnostic stroke work-up in patients with CBI, but without manifest cerebrovascular disease is indicated. Furthermore, this talk will cover the evidence on CBI in patients with manifest ischemic stroke. In stroke patients, those with additional chronic CBI, represent a vascular high-risk subgroup. Location and phenotypes of CBI in stroke patients might even convey clues to the underlying stroke etiology and might inform precision medicine approaches in diagnostics and secondary prevention. The talk will also cover shortcomings of previous studies and directions of future research for this silent pandemic.

Disclosure: The Swiss National Science Foundation (Grant number 32003B_189077) supports a multicentre study on the incidence of silent atrial fibrillation in patients with covert brain infarction, led by our group.

SYMP11-2

The importance of hypertension in secondary stroke prevention

L. Li
Oxford,United Kingdom

High blood pressure is a recognised risk factor for stroke recurrence. In this lecture, we will start with a scoping review on associations of “average” blood pressure and blood pressure variability and various clinical and imaging outcomes after stroke. We will then discuss up to date randomised evidence of blood pressure control in secondary prevention of stroke, focusing both on ischaemic and haemorrhagic strokes and including recruitment updates on ongoing trials in the field. We will move on to discuss some clinically relevant aspects, including ways to monitor blood pressure after the acute phase, when to start treatment, the optimal blood pressure target, and selection of antihypertensive drug class.

Disclosure: Nothing to disclose.

SYMP11-3

Acute stroke management: drip-and-ship or mothership?

M. Ribó
Barcelona, Spain

SYMP11-4

Secondary stroke prevention: identification of underlying cardiac sources of stroke

M. Katan
Zurich, Switzerland

Unfortunately, according to the WHO, stroke is still the second leading cause of death and the leading cause of permanent acquired disability worldwide in 2021. One in four people will suffer a stroke in their lifetime, and once you have suffered a stroke, it is also the most serious risk factor for having another stroke. In the last 20 years there has been progress in preventing new strokes but unfortunately still about 12% will suffer from stroke recurrence within 5 years. This number needs to be improved and we can make a difference ! Secondary prevention after ischemic stroke is based on two main pillars. On the one hand, secondary prevention is based on the identification and treatment of known vascular risk factors such as hypertension, dyslipidemia, diabetes, obesity, and smoking, and on the other hand, on the early identification and thus targeted treatment of the suspected underlying etiology of the stroke that has occurred, but also – even more importantly - of the possible future stroke.

In my talk I will focus on different underlying cardiac diseases as potential sources of ischemic stroke such as atrial fibrillation, PFO but also the concept of atrial cardiopathy. Moreover, I will talk about imaging and blood biomarkers to help better identifying these sources of cardio-embolic strokes and then finally I will talk about current and future treatment options.

Disclosures: I currently receive funding from the Swiss National Science Foundation (142422), the Swiss Heart Foundation and the Baasch Medicus Foundation. I received in kind (assay) contribution for research projects from Brahms Thermofisher and Roche.

Towards personalized Multiple Sclerosis care

SYMP12-1

Imaging methods to predict and monitor individual disease courses

C. Enzinger
Graz, Austria

SYMP12-2

Bodyfluid-biomarkers in multiple sclerosis and related disorders: diagnose, predict, monitor

C. Teunissen
Amsterdam, The Netherlands

Body fluid biomarkers have a great potential to be employed as dynamic and easy implementable tools in clinical practise, to support diagnosis in individual patients, but also for enrichtment and monitoring. Neurofilament light in blood is now an established blood based biomarker, with multiple possible contexts of use for MS and related disorders. I will present recent results of the use of neurofilament light in the clinical context of MS and other neurological diseases (e.g. monitoring, prognosis and enrichment). In addition, recent technological developments create novel opportunities to identify novel body fluid biomarkers for personalised medicine. I will introduce such novel technologies (Olink, Ella), and elaborate how these technologies can help in the development of biomarkers and biomarker profiles. Lastly, I will show examples of their use from our research group.

Disclosure: CT is the primary investigator of a Marie Curie ITN grant, in which diagnostic companies are involved, such as Quanterix, ADx Neurosciences, Olink.

SYMP12-3

Virtual monitoring of MS patients by digital biomarkers – lessons learned from the COVID-19-pandemic

Y. Naegelin
Basel, Switzerland

The COVID-19 pandemic enhances and accelerates an inevitable paradigm shift in interactions between health care providers and patient: from physician guided intermittent clinical visits and assessments towards remote active and passive monitoring and provision of care and education (E-health). The broad availability of electronic/digital tools like smartphones and smartwatches, that have become indispensable in more and more areas of daily life, provides the technological basis for this transformation. Smartphones or smartwatches already contain sensors like accelerometers (acceleration), gyroscopes (angular velocity) and magnetometers (compass level orientation data) that can provide frequent or even continuous, objective, real-world information about qualitative and quantitative aspects of human performance enabling a comprehensive remote assessment. The realization of such obvious advantages and opportunities is not trivial: We need to develop appropriate signal processing and data analysis tools and algorithms to derive informative and reliable features that may be used as "digital biomarkers" out of a nearly indefinite quantity of data. We will discuss challenges and opportunities in the context of ongoing projects that aim at validating digital biomarkers such as our own project "dreaMS". In Multiple Sclerosis (MS), a complex and chronic disease, the additional challenge is to complement established clinical and innovative digital biomarkers by laboratory and imaging features that access the underlying pathological processes in the immune and nervous system. Only such comprehensive approaches will allow real progress towards personalized MS care.

Disclosure: Nothing to disclose.

SYMP12-4

Disease-modifying treatments in MS – how to individualize treatment decisions in daily routine practice?

M. Tintoré
Barcelona, Spain

MS natural history is changing towards are more benign phenotype. A progressive decrease in the time from CIS to MS diagnosis due to changes in diagnostic criteria and a reduction in the time from CIS to treatment initiation have been observed across epoch, and may have contributed to the lower risk of disability accrual that is seen patients diagnosed in more recent epochs. However, aggressive MS still exists and should be identified as early as possible. Current evidence suggests that disease-modifying treatment (DMT) and high efficacy treatments should be initiated at an early stage because it is likely to significantly impact the long term prognosis. Thus, accurately determining the degree of disability that patients are likely develop over the mid- to long-term is crucial for providing more individualized treatment. We will review and stratify which baseline or early demographic, clinical, radiological or biological factors predict disability accumulation. Modifiable factors such as vitamin D, smoking, diet, exercise and comorbidities will be addressed together with the concept of brain reserve and cognitive reserve. We will also present data on a baseline risk score for predicting moderate disability that integrates baseline prognostic factors. We will also discuss the prediction capacity for predicting extremes phenotypes such as aggressive MS defined as reaching an EDSS $\geq$6.0 at 10 years. The development several of risk calculators will be presented.

Disclosure: Compensation for consulting services and speaking honoraria from Almirall, Bayer, Biogen, Genzyme, Jansen, Merck-Serono, Novartis, Roche, Sanofi-Aventis, Viela Bio and Teva

Brain-heart axis and autonomic dysfunction

SYMP13-1

Brain-heart axis and central lesions inducing autonomic dysfunction

M. Hilz
Erlangen, Germany

The cardiovascular system is modulated by the central autonomic network (CAN) which in turn receives information from cardiovascular structures. This interplay assures cardiovascular adjustment to need. Normally, sudden blood pressure (BP) increase augments afferent baroreceptor firing which centrally triggers decreased sympathetic and augmented parasympathetic efferent impulses and initiates swift BP and heart rate (HR) return to baseline. Yet, during efforts, such as stair-climbing, BP- and HR-downregulation would impede adequate muscle perfusion and stair-climbing. Thus, CAN-structures adjust autonomic responses to the actual situation. There seem to be hemispheric differences in cardiovascular autonomic effects. In pre-surgical epilepsy patients, left-hemispheric inactivation augmented sympathetic cardiovascular modulation while right-hemispheric inactivation enhanced cardiovagal activity. Left-sided lesions of the ventromedial prefrontal cortex (VMPFC) which contributes to cardiovascular autonomic responses to emotional stimuli, dampened HR- and BP-adjustment to visual-emotional stimuli, whereas right-sided VMPFC-lesions are associated with exaggerated, paradoxical cardiovascular responses. Insular cortex lesions are associated with increased sudden death. Removal of the amygdalae which contribute to conditioned cardiovascular fear responses decreases sympathetic cardiovascular activation. Conversely, excessive stress may cause myocardial stunning, myofibrillar degeneration, coagulative myocytolysis, or life-threatening arrhythmias. Lesions involving CAN-structures, e.g. due to stroke, multiple sclerosis, or traumatic brain injury, may reduce overall autonomic, particularly parasympathetic modulation resulting in relatively increased sympathetic modulation. Evaluation of the brain-heart interaction is essential to assess the cardiovascular risk of patients with central nervous system diseases.

Disclosures: Dr. Hilz received travel-support and speaker-honoraria from Sanofi, Amicus, Bayer Health Care, consultancy compensation from Sanofi, Alnylam, and Pfizer, and research support from Novartis Pharma.

SYMP13-2

Central ANS dysfunction and brain-heart interactions: from physiological profiling to functional imaging

J. Jordan
Cologne, Germany

In healthy persons, autonomic control centers in the brainstem integrate information from peripheral tissues and higher brain areas to adjust the cardiovascular system to the physiological demands of the body. Functional or structural changes in central cardiovascular control centers have been implicated in various diseases including autonomic failure associated with multiple system atrophy or neurogenic arterial hypertension. Physiological, pharmacological, and biochemical methodologies have been the mainstay to characterize autonomic control mechanisms in human beings. However, approaches to assess the brainstem-heart interactions in human beings have been limited. In the past, functional magnetic resonance imaging has been successfully applied to asses various brain functions, however, brainstem imaging was limited by poor spatial resolution. Conversely, cardiac magnetic resonance imaging lacked temporal resolution required for autonomic research. Therefore, we combined physiological profiling with high resolution functional brainstem imaging or real-time cardiac magnetic resonance. Using the approach, we traced human baroreflex and peripheral chemoreflex regulation at the level of brainstem and hypothalamus. Moreover, we visualized distinct autonomic control circuits in this region. Finally, we established real-time cardiac magnetic resonance imaging to allow for beat-by-beat assessment of right and left ventricular responses to autonomic challenge maneuvers. Now, we apply the approach to elucidate mechanisms mediating cardiovascular autonomic dysfunction in patients with multiple system atrophy, the postural tachycardia syndrome, or neurovascular compression associated with neurogenic hypertension.

Disclosure: Nothing to disclose.

SYMP13-3

Intracranial Pressure and sympathetic activity

A. Pavy-Le Traon
Toulouse, France

The brain modulates cardiovascular function but also receives input from the heart and vascular system that modifies central autonomic output. The relevance of the brain-heart axis is poorly recognized although common neurological diseases such as stroke or traumatic brain injury associate with cardiac rhythm disorders or hypertension. Massive intracranial pressure (ICP) rise leads to cerebral ischemia and is known to produce hypertension, bradycardia and respiratory irregularities due to a sympatho-adrenal mechanism, termed Cushing response. We demonstrated in a group of patients with suspected normal pressure hydrocephalus that ICP is a reversible determinant of sympathetic nervous system (SNS) activity, with experimental confirmation in mice [Schmidt et al 2018].Our data have been confirmed by other independent teams. In patients, 7mmHg ICP rise significantly increases muscle SNS activity by 17%. In live sheep, 10mm Hg ICP rise significantly increases renal SNS activity by 50% [Guild et al 2018]. Hence, independent teams demonstrated brain barosensitivity activating SNS activity and representing a novel "intracranial baroreflex". Astrocytes, that are mechanosensitive, might be a good candidate for being the intracranial baroreceptors. Unlike the extra-cranial carotido-aortic baroreflex, the intracranial baroreflex has a sympatho-excitatory purpose. Modest ICP increase might activate the intracranial baroreflex and participate in the pathogenesis of sympathetic hyperactivity which is involved in the genesis and negative outcomes of many cardio-metabolic disorders such as heart failure, hypertension and obesity.

Disclosure: Nothing to disclose.

SYMP13-4

Neurocardiac axis: Heart'effects on brain in heart failure

C. Arvanitis
Toulouse, France

Heart failure (HF) is a global health challenge that will likely continue to progress in the future due to increased in life expectancy and in acute myocardial infarction survival rates. While we understand the neurohumoral sympathetic activation during HF, it remains unclear how the heart elicits such sympatho-excitation and what role is played by cardiac afferent neuronal fibers. Only in the past few decades have we started to learn about the basic pathophysiology underlying the heart–brain axis. Cognitive impairment is both a critical component of the co-morbidity spectrum of HF and has dramatic consequences in terms of quality of life. Despite the fact that the mechanisms accounting for HF-associated cognitive impairments are unknown, brain hemodynamic changes and adverse drug reactions have been suggested to play a role. There is increasing evidence that the sympathetic nervous system -via the capsaicin-sensitive-afferent sensory nerves- has a cardioprotective role against myocardial ischemic injury. Using a mouse model of HF with cardiac afferent desensitization by local application of resiniferatoxin (RTX), we aimed to evaluate cerebral allostasis through a series of behavioural tests recapitulating different symptoms of depressive disorders. We show the importance of the attenuation of cardiac sensory fibers in alleviating not only cardiac sympathoexcitation but also depression. Discovery of methods that block such activation are critical for the development of improved clinical applications.

Disclosure: This work is in collaboration with INSERM, CNRS, Université de Montréal, and, CHU de Toulouse

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Focused Workshops

Saturday, June 19 2021
MS-related fatigue – tired of inflammation?

FW01-1

Immunological basis of MS-fatigue and therapeutic implications)

T. Berger
Vienna, Austria

Abstract: The etiology of MS-related fatigue is still enigmatic. Apart from the likelihoods of either an association with disrupted sleep architecture thus causing daytime fatigue or with the extent of existing physical disability thus causing fatigue and increased fatiguability by mere exhaustion there might be also a neuroimmunological causative contribution to MS specific fatigue. In this lecture the immune-to-brain communication pathways will be briefly summarized, with emphasis on the response of the central nervous system to peripherally generated chronic inflammatory stimuli – termed as sickness-behaviour in other (mainly infectious) conditions. It will be discussed whether a chronic inflammatory status, specifically mediated by microglia, plays a central role not only in the neuropathology of MS lesion formation but also in triggering MS specific fatigue as a functionally relevant symptom of sickness behavior.
Disclosures: Nothing to disclose.

FW01-2

Functional correlates and diagnostics of fatigue in RRMS/SPMS

I. Penner
Düsseldorf, Germany

Abstract: Fatigue, this overwhelming feeling of tiredness and exhaustion, is one of the most debilitating symptoms of multiple sclerosis (MS). Given the high prevalence rates across all MS-disease courses this symptom has to be taken seriously since it has tremendous effects on patients' daily life, their working ability and finally does also have socioeconomic implications. Although the symptom's existence is undoubted, its exact nature and underlying pathophysiological mechanisms are still a matter of debate. Actually, the diagnostic process is based on patient reported outcomes (PROs) to assess the main clinical presentations, cognitive and motor fatigue. In standard clinical care, these instruments allow structured evaluation, quantification and clinical follow-up of a given individual. However, these instruments only mirror subjective feelings and views of patients and will not be able to allow for causal research. Objective measures are therefore urgently needed to characterize the multifaceted nature of fatigue in more detail and to develop appropriate treatment regimens. At present, only few functional correlates have been detected which in turn can be attributed to the conceptual heterogeneity and uncertainty what fatigue really means. The most plausible functional explanation is based on imaging results suggesting a disconnection between certain cortical and subcortical structures involving prefrontal cortex, basal ganglia, and thalamus. In addition, proinflammatory cytokines as well as neuroendocrine dysregulation have been related to the pathogenesis of fatigue. However, despite the growing number of research in the field, no clinically useful biomarker has been proposed and established so far.
Disclosure: Honoraria for speaking at scientific meetings, serving at scientific advisory boards and consulting activities from Adamas Pharma, Almirall, Bayer Pharma, Biogen, Celgene, Desitin, Sanofi-Genzyme, Janssen, Merck, Novartis, Roche, and Teva.

FW01-3

MS-Fatigue from a somnologist's perspective

S. Knudsen-Heier
Oslo, Norway

New therapeutic approaches in rare neurological diseases

FW02-1

Transition from paediatric to adult care: Treatments for rare diseases the adult neurologist needs to know about.

U. Schara-Schmidt
Essen, Germany

Abstract: Background: Neurological disorders in childhood, adolescence and adulthood are rare and very rare diseases; for many, prevalence and incidence are unknown. Causal therapies are currently used only for individual disease identities. Nevertheless, new genetic methods, a better understanding of pathophysiology and multidisciplinary treatment concepts are improving patients` life expectancy and quality of life. As a result, patients with an early disease onset reach adulthood and further care in adult medicine is necessary. Often, Neurology is the leading discipline.
Question: How can transition be made meaningful? Where do problems stand out?
Material and method: Using examples of disorders transition should be presented and important aspects and possible problems pointed out.
Conclusions: The transition process is complex and requires time and personnel resources. If carried out sensibly, it can lead to an efficient care of patients in the long term and thus be also economically effective.
Disclosure: Nothing to disclose.

FW02-2

Rare neuromuscular disorders: from precise diagnosis to personalized treatment

T. Evangelista
Paris, France

Abstract: In Europe there is an estimated 30 million people affected by more than 7,000 rare diseases (RD); around 80% of genetic origin. Most rare diseases and in particular rare neurological diseases still lack approved treatments in spite of major research advances in the understanding of the molecular basis of diseases. A key aspect to translate advances in disease knowledge into potential medicines is a careful selection of the therapeutic modality to be developed (e.g. small molecules, monoclonal antibodies, protein replacement therapies, gene and cell therapies, or drug repurposing). We will summarize the main aspects of different novel therapeutic approaches with some examples of success stories. The RD world is quite specific in its characteristics and it has to face different challenges and opportunities to be able to develop and approve therapies. We will briefly discuss the current challenges and opportunities in this domain such has trial design, data sharing, patient engagement or regulatory pathways. The European Reference Networks provide a needed opportunity to coordinate RD research in order to improve standards of care, increase access to diagnosis and treatment, increase the understanding of phenotypes and natural history, increase enrolment of patients into clinical trials, and create disease registries.
Disclosure: The author is a member of the European Reference Network for rare neuromuscular diseases (EURO-NMD) – Project ID No 739543.

FW02-3

Rare and complex epilepsy syndromes: from precise diagnosis to personalized treatment

E. Trinka
Salzburg, Austria

Etiology-driven therapy in epilepsy: From bedside to bench

FW03-1

Neuroinflammation in epilepsy: not only autoimmune encephalitis

M. Carreno
Barcelona, Spain

FW03-2

Genetics in epilepsy: not only abnormal channels

S. Zuberi
Glasgow, United Kingdom

FW03-3

mTOR pathway in epilepsy: not only Tuberous Sclerosis Complex

R. Guerrini
Florence, Italy

The role of the muscle acetylcholine receptor isoforms in myasthenic syndromes

FW04-1

Reduction of the safety factor in myasthenic syndromes

H. Cetin
Vienna, Austria

Abstract: The reliability of neuromuscular transmission is described by the concept of safety factor, and determined by various structural and molecular adaptations of the neuromuscular junction. In general, the safety factor defines how much larger than required an effect of the presynaptic nerve terminal has to be to generate an action potential in the muscle fibre, ensuring that each nerve action potential is translated into a muscle action potential under physiological conditions. Different factors including i) the release of a substantially high number of presynaptic vesicles, ii) high acetylcholine receptor and voltage-gated sodium channel densities at the postsynaptic membrane and iii) the increase of input resistance at the postsynaptic region by muscle membrane folds contribute to the safety factor that is around 2 in human. In myasthenic syndromes, autoantibody-mediated mechanisms targeting pre- and postsynaptic proteins or mutations affecting the function of these proteins compromise the safety factor and impair neuromuscular transmission. Extraocular muscle fibres are characterised by a lower safety factor as compared to limb muscles, resulting in a higher susceptibility of extraocular muscles to weakness in myasthenia gravis and in some genetic forms of myasthenic syndromes. Higher motor neuron firing frequencies were recently proposed to further contribute to a lower safety factor by increasing the release of acetylcholine from the presynaptic terminal and resulting in the accumulation of acetylcholine receptors in desensitised states. The understanding of mechanisms defining the safety factor and underlying disease states is important to direct the clinical management of patients with autoimmune and genetic myasthenic syndromes.
Disclosure: Nothing to disclose.

FW04-2

Fetal and adult AChRs in congenital myasthenic syndromes

D. Beeson
Oxford, United Kingdom

Abstract: In early biochemistry studies of mammalian muscle denervation it was evident that acetylcholine receptors (AChR) with different properties existed. Confirmation came with the cloning of cDNA encoding the ε- and γ-subunits from calf muscle and the demonstration that inclusion of the ε- and γ-subunit into the AChR pentamer underlies the differing properties. The adult isoform (α2βδε) and the fetal isoform (α2βγδ) differ in their developmental expression profile, electrophysiological properties of channel conductance, open time and Ca2+ permeability, and in their affinities for choline and acetylcholine. Despite it now being over 30 years since the properties of the two AChR isoforms were defined there is still debate about their precise biological role and why two muscle AChR isoforms evolved. In this presentation I will review the differing human phenotypes (congenital myasthenic syndromes) that result from mutations within the AChR ε- and γ-subunits, the biological information we can gain from detailed characterisation and the implications for treatment. The majority of what we know about muscle AChR comes from studies of rodent neuromuscular junction and it is tempting to think functional studies of neuromuscular transmission in the mouse can be directly translated to humans, however the congenital myasthenic syndromes teach us to be cautious with this approach. In particular, the expression profile for the AChR ε- and γ-subunits is very different, has a marked impact on phenotype, and needs to be taken into account when developing disease models.
Disclosure: Nothing to disclose.

FW04-3

Fetal and adult AChRs in autoimmune myasthenic syndromes

A. Vincent
Oxford, United Kingdom

Abstract: Possible differences between the structure/function of acetylcholine receptors during development and at the mature neuromuscular junction were recognized early (reviewed in Vincent, Nature News & Views 1975). Subsequently, it became clear that the gamma (fetal-specific) subunit was replaced by an epsilon (adult-specific) subunit during muscle development. Most patients with myasthenia gravis have antibodies that bind to the two alpha subunits and which do not, therefore, distinguish between the two isoforms. However, many MG patients do have some fetal AChR specific antibodies perhaps because the fetal isoform is the predominant form in the thymic myoid cells and are involved in the immune response. In the 1990s, we and others detected fetal-AChR specific antibodies in mothers of children with arthrogryposis multiplex congenita, some of whom were asymptomatic. Fetal-AChR specific antibodies could be cloned from B cells in the thymus of two of these mothers and were more common in parous women, irrespective of the outcomes of the pregnancies (Matthews et al 2002), suggesting that antibodies may also be stimulated by fetal cells or antigens that reach the mothers' circulation during pregnancy. In addition, it is now clear that some surviving children from similar mothers, despite not having severe arthrogryposis, have a persistent facial myopathy. Using an established mouse maternal–to-fetal transfer of human antibodies (Jacobson et al 1999) we have shown that transfer of potentially pathogenic fetal-specific AChR antibodies can be reduced in order to protect the developing fetus (Coutinho et al 2021).
Disclosure: Nothing to disclose.

From precision medicine to the use of artificial intelligence in neurointensive care

FW05-1

Multimodal neuromonitoring to guide precision medicine in neurocritical care

S. Wolf
Berlin, Germany

FW05-2

Artificial Intelligence in neurocritical care

N. Schweingruber
Hamburg, Germany

Abstract: Artificial Intelligence (AI) is introduced to medicine and an AI assistance will be the future that we should help to shape. Supervised, unsupervised, and reinforcement learning will be the main methods to play role in the implementation of AI. Severely ill patients admitted to intensive care unit are monitored closely to early detect deterioration. This monitoring data can be used to train AI models to predict critical phases in advance, making an earlier reaction possible. To achieve this a lot of clinical data is needed and an external validation on independent cohorts should take place. Prospective studies with treatment of patients admitted to ICU with AI assistance should show that they provide a benefit for patients. To introduce the advantage of AI in clinical routine in the future, more AI based models with larger datasets will be needed. To achieve this international cooperation are mandatory. Clinical centers associated with universities are needed to provide a constant validation of applied models and detect potential declines of performance during clinical implementation.
Disclosure: Nothing to disclose.

FW05-3

Ethico- legal aspects of artificial intelligence in neurocritical care)

B. Arda
Ankara, Turkey

Abstract: By the mid-20th century, the impact of technology on medicine had become very evident. On the one hand, physicians were starting to lose their ancient "techne oriented" professional identity. On the other hand, a new patient type emerged; as a figure demanding her/his rights, beginning to inquire about the physician's paternalism. Even in this case, it was inevitable that different approaches would replace traditional medical ethics. Currently, these new approaches are challenged once more with the emergence of AI in healthcare. The main question is how the patients and caregivers will be shaped within the medical ethics framework in the AI world?
Disclosure: Nothing to disclose.

Infections as triggers on autoimmunity

FW06-1

Infections as triggers of autoimmune encephalitis and related disorders

S. Muñiz Castrillo
Bron Cedex, France

Abstract: The initial trigger leading to the immune tolerance breakdown is still unknown in most autoimmune encephalitites associated with antibodies targeting neuronal surface antigens. Nevertheless, prodromal symptoms compatible with mild infections are not infrequent, suggesting that some common and benign microbiological agents could act as triggers of the autoimmune reaction. Conversely, herpes simplex virus (HSV) encephalitis is now a well-characterized trigger of autoimmune encephalitis, and is particularly related to the development of anti-NMDAR antibodies, though other specificities have also been reported. Serological studies as well as an animal model further support the association between HSV and anti-NMDAR encephalitis, but the underlying pathogenesis is still obscure. However, a genetic predisposition involving the Toll-like receptor 3-pathway might exist at least in a subset of patients. In addition to HSV, anti-NMDAR and other autoimmune encephalitis have also been associated with other infections, chiefly Japanese encephalitis and HIV, but new epidemic and pandemic diseases such as COVID-19 are raising concern as potential triggers of autoimmune encephalitis. On the contrary, despite the recent description of anti-neural antibodies against different targets in some patients, solid evidence regarding the autoimmune pathogenesis is still lacking for several historically reported post-infectious neurological diseases, such as Sydenham chorea and von Economo´s encephalitis lethargica. Interestingly, type 1 narcolepsy constitutes a good example of neurological autoimmunity triggered by infection in genetic susceptible subjects that might provide some clues for future research in autoimmune encephalitis.
Disclosure: Nothing to disclose.

FW06-2

Infections as triggers of other central nervous system autoimmune disorders

D. García Azorín
Valladolid, Spain

Abstract: Infectious diseases are often included in the differential diagnosis of many neurological disorders and syndromes. Besides the central and peripheral nervous system manifestations of microbiological agents, such as Zika virus, varicella zoster virus, herpes virus, Malaria, Epstein-Barr virus, West Nile virus influenza virus or recently severe acute respiratory syndrome coronavirus 2. Postinfectious manifestations of these agents cover autoimmune syndromes, including opsoclonus-myoclonus, cerebellitis, myelitis, acute demyelinating encephalomyelitis, and Bickerstaff brainstem encephalitis, among others. The frontier between acute and postinfectious is not always evident. The key diagnostic features will be summarized, including disease-specific antibodies, as anti-GQ1b in Bickerstaff encephalitis; and which ancillary exams might disentangle the presence of an acute infection or the evidence of a passed infection, such as oligoclonal bands or immunoglobulin M/G in serum or cerebrospinal fluid analysis. To date, different treatments have been proposed, including steroids, intravenous immunoglobulins, plasmapheresis or other immunotherapies, however evidence is limited, and evidence is relatively weak for most therapeutic options.
Disclosure: Nothing to disclose.

FW06-3

Infections as triggers of Guillain-Barré syndrome

J. Sellner
Mistelbach, Austria

New developments in understanding disorders of language

FW07-1

Language symptoms and testing, in aging, aphasia and cognitive decline

I. Pavão Martins
Lisbon, Portugal

Abstract: Language complaints and disturbances are frequent in the clinical practice, particularly after focal and degenerative disorders, where they can be the first manifestation of the disease. Although clinicians still tend to dichotomize language in expressive and comprehension impairments, this traditional approach is no longer consistent with what we know about language organization, since single regions can be involved in the decoding and production of the same linguistic information. Neuroimaging of large series of patients and connectivity based parcelation studies have expanded our understanding about the architecture of language circuits, within, between and beyond the classical areas described by Broca and Wernicke. Moreover, neurophysiologic studies are unravelling network dynamics during speech processing in real time. In this workshop we will review language symptoms and disorders according to these new perspectives and indicate the type of clinical assessment that will target specific disturbances. We will discuss the dual processing model, consisting on ventral and dorsal language pathways related to acoustic-articulatory mapping and lexic-semantic processing, respectively, and the type of language errors resulting from dysfunction of each stream. We will also present disorders of fluency, speech programming and subtypes of semantic disturbances. Finally, we will underline the type of subjective language complaints associated to normal aging. We expect that the workshop attendees will update their knowledge on language disorders and language network organization, will be able to indentify language impairments in degenerative diseases and to select the most appropriate tools to assess the different types of language complaints.
Disclosures: Nothing to disclose.

FW07-2

Language disorders in neurodegenerative diseases

C. Cerami
Pavia, Italy

Abstract: Language impairments play an increasingly important role in the identification and diagnosis of many neurodegenerative diseases. In addition to primary progressive aphasia (PPA), several other neurodegenerative disorders within frontotemporal lobar degeneration, Alzheimer's disease (AD) and α-synucleopathy spectrum may show impairments at language tests, even in the early stages. Various degree of impairments in tasks exploring different language domains, such as phonology, semantics and syntax, may thus be present in the behavioral variant of frontotemporal dementia (bvFTD), the progressive supranuclear palsy (PSP), the corticobasal syndrome (CBS), the posterior cortical atrophy (PCA) or the Lewy bodies dementia (LBD). Efficiency in executive functions and working memory plays a critical role in speech and language performances in bvFTD, PSP and lvPPA, while visuo-perceptual and visuo-spatial abilities can influence performances at language tasks with a visual input in PSP, CBS and PCA. Graded variations of language symptomatology can be detected across neurodegenerative syndromes sharing same or different pathological substrates (e.g., phonological impairments are core features of the logopenic variant of PPA but may also be present in CBS and PCA). Structural and functional connectivity derangements of complex brain networks subserving different language domains have been demonstrated to play a key role. Nonetheless, language profiles and the respective neural correlates have been only partly elucidated and further studies are needed to explore inter- and intra-variations of language performances among different neuropathological groups.
Disclosure: Nothing to disclose.

FW07-3

Language Connectomics

M. Thiebaut de Schotten
Bordeaux, France

Sunday, June 20 2021

Precision medicine in stroke - where are we?

FW08-1

Precision medicine in stroke - Current applications

S. Lorenzano
Rome, Italy

Abstract: Precision medicine represents the future for improving primary/secondary prevention,diagnosis, phenotyping, and outcome determination. Expanding precision medicine to the stroke area in order to identify diagnostic and prognostic markers is crucial although challenging. The implementation of this concept in clinical practice is still far from being a reality and healthcare disparities could limit the acceleration of translation from the science of precision medicine into clinical practice around the world. To achieve this goal,new approaches and strategies along with novel technologies,informatics and identification of practical clinical paradigms need to be implemented. The great amount of data from clinical trials,population studies, routine care, databases,registries, including clinical,cognitive, advanced neuroimaging (including metabolic imaging, imaging of functional connectivity, radiomics) data, omics (genomics/transcriptomics/proteomics/metabolomics) findings as the basis for integromics and system biology, and data from clot composition analysis should be shared across centers, collected using standardized methods and a high-quality big-data approach, and made available as a fertile ground for future studies.Furthermore, the use of artificial intelligence/machine learning could allow the development of algorithms that, if validated,may guide stroke physicians in tailoring decision-making process regarding patient selection, prognosis determination, and prevention strategies for each individual patient. This obviously needs expertise and multidisciplinary approaches including stroke clinicians and both clinical and basic researchers, data scientists,omics specialists, biostatisticians, epidemiologists, computer scientists/engineers, and experts in advanced analytics and artificial intelligence. Multicenter collaborative efforts should be put in place through the establishment of consortia and adequate infrastructure for proper and standardized data collection. What is certain is that a philosophic and paradigm shift in the stroke community should occur because individualized treatments represents the next frontier.

Disclosure: Dr. Lorenzano served as expert consultant for Boehringer Ingelheim (2013–2014); received two travel grants from Boehringer Ingelheim (2016/2017); one from Bayer (2014), Quintiles IMS and Daichii Sankyo (2017) for meetings/conferences

FW08-2

Future applications

A.C. Fonseca
Lisbon, Portugal

Abstract: Precision medicine is broadly defined as tailored diagnosis and therapy for each individual patient. From an initial standpoint where treatment for a disease was needed and therefore an “one-size-fits-all” approach was used we are now changing to a tailored approach with treatment suited for the particular characteristics of each individual. Advancement and application of precision medicine to stroke medicine in the future will hopefully lead to a better and individualized care of stroke patients. This will contribute to the reduction of the burden of stroke. Advanced brain imaging methods are starting to helps us to know more about individual thresholds to brain ischemia and to personalize therapeutic time windows for endovascular treatments. A review of the ongoing studies and of the different biomarkers that are being studied will be provided. The expectation is that the use of different types of biomarkers will in the future, enhance early stroke diagnosis and estimation of prognosis that will allow an adapted treatment for each patient

Disclosure: Nothing to disclose.

FW08-3

Precision medicine or personalized medicine?

L. Caplan
Boston, United States of America

Abstract: Precision refers to a mode of action- being exact and accurate, while personalized refers to attention to an individual person. Optimally treatment should be both precise and personalized. Each individual is different. Patients live in a very complex social, civic, cultural, economic, religious, and philosophic environment. Treating physicians must understand and diagnose the cause of the patient’s symptoms and illness in as much detail as possible. They also must understand the person and the milieu. A very detailed history, physical and neurological examination, laboratory testing, and technological advances in brain and vascular imaging now make it possible for physicians to acquire the data needed to be able to direct management to complex individual patients. Randomized trials, the basis of so-called evidence-based medicine, yield general information but often do not provide a road map to treat individual patients.

Disclosure: Nothing to disclose.

EAN/EUGMS Emerging and future diagnostics in Alzheimer's disease and dementia

FW09-1

Dynamic changes in awareness for cognitive decline and EEG: affordable markers of preclinical AD

S. Epelbaum
Paris, France

FW09-2

Plasma biomarkers in dementia: past, present and future

F. Bouwman
Amsterdam, The Netherlands

Abstract: This presentation will cover past developments in plasmabiomarkers for neurodegeneration especially Alzheimer's disease. Current neurodegenerative plasma-biomarkers reported on in literature that have good diagnostic quality wil be discussed as well as it's challenges for application in future
Disclosure: Nothing to disclose.

FW09-3

Genetics of the dementias – from autosomal dominant disease to pre-symptomatic screening

J. Schott
London, United Kingdom

Abstract: A small but significant proportion of cases of dementia are caused by autosomal dominant mutations. Identification of a causal mutation allows for a definitive diagnosis to be made in life and appropriate counselling and support to be offered to patients and family members; is the basis for reproductive choices including in selected cases preimplantation genetic diagnosis; and allows access to research and clinical trials. The likelihood of identifying a specific genetic cause of dementia depends on the clinical condition, the age at onset and family history: in many cases there is significant overlap between genotype and clinical phenotype. The advent of new genetic technologies allows for multiple genes to be assessed in parallel, but also means that clinicians are confronted by variants of uncertain significance or unexpected findings. Particularly given the potential implications for family members, genetic testing needs careful explanation and discussion with patients and family members. In this lecture I will give a neurologist's overview of how to approach genetic testing for dementia in clinical practice
Disclosure: Nothing to disclose.

EAN/MDS-ES Experimental therapies for rare movement disorders

FW10-1

Experimental Therapies for Huntington's Disease

A. Rosser
London, United Kingdom

Abstract: Huntington's disease (HD) is an inherited neurodegenerative condition, resulting in progressive impairment of cognition, behaviour and movement, and predominantly associated with degeneration of medium spiny striatal neurons (MSNs). The underlying cause is expansion of a CAG repeat sequence in exon 1 of the huntingtin gene, leading to expression of a mutant form of the huntingtin protein. There are currently no disease-modifying treatments and few meaningful symptomatic treatments, but a number of experimental therapies are being actively explored, with the most prominent currently being attempts to lower brain levels of mutant huntingtin protein through the use of antisense oligonucleotides or gene therapies. Several non-huntingtin lowering approaches have also reached clinical translation, one being attempts to replace degenerated striatal MSNs through transplantation of MSN progenitors into the adult striatum. Animal studies have demonstrated the capacity of such cells to establish appropriate synaptic connections, and a number of small studies in patients with HD have demonstrated safety, feasibility and provided proof of principle that cell therapy can improve function. However, there are still many gaps in our knowledge relating to the underlying mechanisms by which fetal donor cells exert effect on the host brain and the conditions required to achieve more reliable efficacy. These need to be addressed through an iterative process using animal models and human studies. As many potential disease-modifying agents do not cross the blood-brain barrier, it is timely to address the common challenges of delivering molecules and cells directly to the brain in HD.

Disclosure: I have provided consultancy services for Roche, Wave Life Sciences and Triplet Therapeutics. I am Chair of the European Huntington's Disease Network, which is supported by a grant from the CHDI Foundation.

FW10-2

Experimental Therapies for Rare Movement Disorders – MSA

W. Meissner
Bordeaux, France

Abstract: Multiple system atrophy (MSA) is a rare and fatal neurodegenerative disorder characterized by a variable combination of parkinsonism, cerebellar impairment, and autonomic dysfunction. The pathologic hallmark is the accumulation of aggregated α-synuclein in oligodendrocytes forming glial cytoplasmic inclusions, which qualifies MSA as a synucleinopathy together with Parkinson's disease and dementia with Lewy bodies. α-synuclein is currently the main target for the development of possible disease-modifying treatments for MSA. In this regard, enhancing the clearance of α-synuclein via autophagy (transcription factor EB) or direct proteolysis (neurosin), inhibiting its aggregation (anle 138b and CLR01) or post-translational truncation (belnacasan), as well as active (Affitope PD01A) and passive immunotherapy (CD5-D5) have demonstrated beneficial effects on motor behavior, α-synuclein burden and other neuropathological readouts in transgenic MSA mice. Additional compounds targeting muscarinic receptors, insulin resistance, Toll-like receptor 4 and histone acetylase have also shown beneficial effects in transgenic mouse models of MSA. These preclinical results have motivated the conduction of a phase I trial to evaluate the safety and tolerability of repeated administrations of specific active immunotherapy against α-synuclein with Affitope PD01A and PD03A (NCT02270489). Both vaccines were safe and well tolerated. It is very likely that additional strategies targeting α-synuclein will be evaluated in MSA patients within the next few years. In this regard, a phase I trial to assess the safety and tolerability of anle138b in healthy volunteers is currently ongoing (NCT04208152). Additionally, a small phase II trial with exenatide (NCT04431713), an approved antidiabetic, is ongoing.

Disclosure: Fees for editorial activities with Springer Nature and Elsevier, consultancy fees from Lundbeck and Biohaven, and teaching honoraria from UCB.

FW10-3

Experimental therapies for progressive supranuclear palsy

G. Hoeglinger
Hannover, Germany

Abstract: Progressive supranuclear palsy (PSP) is a neurodegenerative disease with predominant 4R-tau aggregates. PSP has a wide spectrum of clinical presentations. The typical clinical presentation of PSP is called Richardson´s syndrome. Clinical features include ocular motor dysfunction and postural instability. A number of other syndromes associated with PSP pathology have been described in the literature. These include syndromes with predominant motor manifestations, such as PSP with parkinsonism, as well as syndromes with predominant cognitive manifestations, such as PSP with frontotemporal dementia. The clinical phenotype is primarily driven by the topography of cerebral tau pathology. Several factors contribute to dysfunction and aggregation of the tau protein, ultimately leading to neurodegeneration. A broad spectrum of therapeutic approaches is currently under development. Reduction of MAPT translation with antisense oligonucleotides thus represents a possible treatment strategy for tauopathies. Splice modifiers acting on exon 10 may restore this balance as possible therapeutic approach to tauopathies. Several approaches to alter posttranslational modifications of tau (e.g. covalent binding of O-linked N-acetylglucosamine or phospho-residues) are being developed to stabilize the affinity of tau to microtubules and to prevent aggregation of tau. Preventing release and uptake of tau, as well as promoting tau clearance in the extracellular space, are being considered as therapeutic strategies to reduce the propagation of tau pathology. Spreading-competent extracellular tau as targets for tau antibodies is being studied in clinical trials employing both active or passive immunization approaches. This presentation will provide an update on the pathophysiological concepts and experimental therapies for PSP.

Disclosure: Consultant for Abbvie, Alzprotect, Asceneuron, Bial, Biogen, Biohaven, Lundbeck, Novartis, Roche, Sanofi, UCB; Honoraria for presentations from Abbvie, Bayer Vital, Bial, Biogen, Bristol Myers Squibb, Roche, Teva, UCB, Zambon.

Focus on Biomarkers in Common Diseases?

FW11-1

Genetics: What are the "true" genetic biomarkers in neurological disorders

N. Wood
London, United Kingdom

FW11-2

Body fluid markers: recent developments

B. Giometto
Trento, Italy

Abstract: Laboratories are expected to play a key role in the diagnostic workup of suspected Neurological Disorders where screening tests are available for antibodies and classical serological or CSF markers. The diagnostic approach to a patient with a suspected Neurological Disease can be challenging and involves an accurate evaluation of symptoms, clinical findings, laboratory tests and imaging.
Clinical signs suggestive of a neurological syndrome attributable to an Autoimmune or Paraneoplastic Disorder raise two diagnostics issues: correct diagnosis of a specific PNS and the marker requested, and identification of a possible concomitant malignancy and its location. The presence of antibodies, especially Neuronal Surface or Onconeural Abs, increases the probability that the neurological syndrome is Autoimmune and studies are available to inform and assist clinicians in the appropriate use of antibody tests. Detection of a possible underlying malignancy is more challenging as the presence of antibodies is associated with a risk rate, which is difficult to apply in making decisions on the individual patient. Circulating onconeural Abs are commonly considered a valuable tool for cancer diagnosis and are frequently requested in clinical practice for patients with unclear neurological symptoms. To take appropriate decisions, the clinician should usually rely on clinical practice guidelines. However, recommendations provided by clinical practice guidelines may not cover all clinical questions or may not be consistent across guidelines produced in different contexts. Proper adherence to use of biomarkers by physicians is critical for translating guideline recommendations into improved healthcare
Disclosure: Nothing to disclose.

FW11-3

Neuroimaging: Impact on treatment decisions and disease monitoring

M. Smits
Rotterdam, The Netherlands

Abstract:
Imaging plays a central role in the management of patients with neurological disease, with MRI being the optimal modality due to its excellent tissue contrast and non-invasiveness. Clinically, MRI is primarily qualitatively, based on subjective interpretation of gross imaging features. Recent advances in image acquisition and analysis technology, however, are moving the field of Radiology forward towards quantitative imaging and imaging biomarker development. Advanced imaging techniques provide quantitative structural and physiological measures of tissue properties. Computational analysis of radiographic imaging has resulted in the rapidly evolving field of radiomics, which correlates large numbers of quantitative imaging features with tissue properties and clinically relevant disease characteristics and patient outcome.
In this lecture I will describe how commonly used MRI techniques can be applied quantitatively and can be developed into imaging biomarkers. I will furthermore highlight some of the promising MRI techniques that are currently being researched for their clinical application. Finally, I will discuss the background and use of radiomics. The focus will be primarily on neuro-oncology, but the main principles are applicable to other neurological diseases.
Disclosure: Speaker fees from GE Healthcare – paid to institution.

EAN/ISNI Immune checkpoint inhibitors: a step towards precision neurology

FW12-1

Friends: ICIs as possible treatment for infectious diseases of the CNS

G. Martin-Blondel
Toulouse, France

FW12-2

Friends: ICIs as potential treatment in Neuro-Oncology

S. Oberndorfer
St. Pölten, Austria

Abstract: One of the hallmarks of cancer is to overcome immunosurveillance and the capability of cancer cell to co-opt immune checkpoint pathways. Immunological approaches of cancer treatment including immune checkpoint inhibitors (ICI) initiated a new area in many fields of oncology. Beginning with the successful treatment of metastatic melanoma with ICI, many improvements with respect to disease control could be achieved in several cancer types including lung cancer, renal cell carcinoma, bladder cancer, ovarian cancer, gastric cancer and many others. However, the major impact of ICI in the field of Neuro-Oncology to date is the observation of a completely new spectrum of neurological side effects from anticancer treatment. With respect to brain tumor treatment, ICI only revealed efficacy in brain metastases of melanoma and lung cancer. With respect to glioma, treatment success is still limited. Although different treatment algorithms for glioma, including combination therapies with ICI have been conducted, results showed no convincing results so far. A long list of factors may contribute to the lack of efficacy in the treatment of glioma with ICI, such as the tumor microenvironment, as well as multiple patient and iatrogenic factors. In order to pave the way for immunotherapy in Neuro-Oncology, all these factors need to be studied in more detail to understand the immunological mechanisms of the unique microenvironment of the CNS. Moreover, future trials need to establish robust biomarkers in order to identify potential subgroups of brain tumor patients who may benefit from immunotherapy with ICI.
Disclosure: Nothing to disclose.

FW12-3

Foes: Neurological toxicities related to ICIs

A. Vogrig
Udine, Italy

Abstract: Given their efficacy in many types of cancer, immune checkpoint inhibitors (ICIs) are increasingly used in oncology. ICIs have a spectrum of toxicities that is different to classic chemotherapy, including neurologic immune-related adverse events (n-irAEs). Serious n-irAEs are rare (1–3% of patients) but are important since they can lead to disability or death. Their frequency varies according to the number of ICIs adopted (higher in combination regimens) and the type of ICI (higher using anti-CTLA-4 antibodies). Neuromuscular complications account for three quarter of the cases, and the most common toxicities in order of frequency are myositis, Guillain-Barré syndrome, and myasthenic syndromes. Importantly, these complications have some differences with their classic counterparts (e.g. ICI-triggered myasthenia gravis often present with concomitant myositis, respiratory insufficiency, and myocarditis). Central nervous system disorders are less frequent, and three main patterns were described: limbic encephalitis, meningoencephalitis, and cerebellitis, each with a distinct immunological background, disease evolution and response to treatment. Some patients, especially those receiving combination regimens, develop cranial neuropathies, which can be bilateral, show gadolinium-enhancement of the affected nerves, and can lead to persistent sequelae, most frequently involving hearing and vision loss in one third of the patients. Intriguingly, clinically relevant differences exist between ICI adopted, associated cancer, and neurological phenotype. Anti-PD-1/PD-L1 are more frequent in myasthenic syndromes and less common in meningitis and cranial neuropathies, while anti-CTLA-4 are more common in meningitis and less frequent in encephalitis and myositis. Herein, we provide a comprehensive review of the diagnostic approach and management of n-irAEs.
Disclosure: Dr. Vogrig reports receiving a fellowship grant from the EAN.

EAN/PNS: Forty years of anti-nerve antibodies in neuropathy: still moving on

FW13-1

Anti-MAG antibodies

L. Querol
Barcelona, Spain

FW13-2

Anti-ganglioside antibodies

H. Willison
Glasgow, Scotland

Abstract: In human autoimmune neuropathies, studies investigating humoral effector mechanisms conducted during the last 40 years have focused heavily on serum anti-ganglioside antibodies, now described in over 1,000 publications. Gangliosides including GM1, GD1a and GQ1b are a family of around 50 structurally distinct sialic acid-containing glycosphingolipids that perform essential biological functions throughout the body, most notably in the nervous system. Non-ganglioside glycolipids including sulfatides, galactocerebroside, LM1 and SGPG are also important neural antigens in a wide variety of neuropathy settings. Despite our tremendous advances in knowledge, this field remains complex and incomplete, in large part because of the profound practical and conceptual difficulties in investigating glycolipids in the clinically relevant physiological and pathological setting of human peripheral nerve. The highly ordered membrane domains in different nerve compartments display ganglioside oligosaccharides to the extracellular environment in a range of different patterns subject to local topographical constraints. Cis-interactions between adjacent glycolipids introduce enhancing and inhibitory influences on antibody binding. Neural injury can be exaggerated or attenuated by variations in the levels of ganglioside target and their accessibility in nerve compartments, for example the nodal and internodal axolemma. A major unsolved question for the future remains the nature of the putative glycolipid antigen(s) that mediate the common-or-garden demyelinating forms of GBS and CIDP. This presentation reviews some of the conceptual considerations and experimental highlights in this field.

Disclosure: Nothing to disclose.

FW13-3

Anti-paranodal proteins antibodies

C. Sommer
Würzburg, Germany

Abstract:
Autoantibodies against paranodal proteins define a subgroup of inflammatory neuropathies, mostly classified as a subtype of chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). IgG4 autoantibodies against the paranodal protein neurofascin-155 characterize a group of patients with pareses, tremor and ataxia, and poor response to IVIG or other standard CIDP treatment. Antibodies to contactin-1 can be associated with a similar syndrome, and, in addition, glomerulonephritis. Patients with antibodies to caspr-1, in addition, may suffer from severe pain. Complement-fixing IgG3 antibodies targeting paranodal proteins have also been described and may reflect an earlier phase of the disease, as in acute-onset CIDP. Demyelinating features in the nerve conduction studies but an axonal histological phenotype are typical for the "paranodopathies". Pathogenicity of the antibodies has been shown in passive transfer studies for some of the antibody subtypes. Although there are no formal clinical trials, all case report published so far report an excellent response to treatment with rituximab. A very severe phenotype of neuropathy, sometimes requiring intensive care treatment for several months, ensues if antibodies to all subforms of neurofascin (NF155, NF186, NF140) are present.

Disclosure: Consulting or educational talks regarding immune neuropathies for Immunic, Roche, UCB, Merck, Grifols, and CSL Behring.

Monday, June 21 2021
Migraine diagnosis in the era of precision medicine

FW14-1

Improving clinical diagnosis of migraine

R. Gil-Gouveia
Lisbon, Portugal

Abstract: There are no genetic, laboratorial, neurophysiological or imaging biomarkers available to confirm the diagnosis of migraine, that is supported by consistent clinical criteria defined in the International Classification of Headache Disorders. In most cases, migraine diagnosis is straightforward and presumptive diagnosis can even be assumed with the use of simple screening tools, such as ID- Migraine©. So, migraine is of fairly easy diagnosis, all you need is a knowledgeable physician. Such a physician recognizes that the migraine syndrome has many symptoms not included in the diagnostic criteria, that frequently migraine patients may not present all the cardinal symptoms or, most likely, may have other less common symptoms that cast confusion or doubts in establishing the correct diagnosis. Understanding the syndrome, its temporal patterns and natural history is relevant not only for diagnosis, but to adapt therapeutic strategies and to understand brain processes involved in each symptom or migraine phase. In the new era of precision medicine, we need to get back to the basics and take time to listen to our patients to learn about each patients' migraine, to understand the pathophysiological mechanisms in place so we can be alert to adapt our diagnostic ability and therapeutic strategies to each patients' needs.
Disclosure: No conflicts of interest regarding this talk. Conferences/ Consulting or Meetings from ALLERGAN, BIOGEN, BOHERINGER, DAIICHI SANKYO, LILLY, LUNDBECK, NOVARTIS, SANOFI and TEVA; Research Grants FCT (Portugal 2020), 29675 and Novartis-SPC.

FW14-2

Advances in Genetics for migraine diagnosis

N. Pelzer
Leiden, The Netherlands

Abstract: Migraine is a known heritable disease with increased familial occurrence. In autosomal dominant familial hemiplegic migraine, which can also occur sporadically, a single pathogenic mutation in CACNA1A, ATP1A2 or SCN1A can confirm the clinical diagnosis. If migraine occurs with a family history of cerebrovascular disease, several monogenic cerebral hereditary angiopathies can be diagnosed by genetic testing, including cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL), retinal vasculopathy with cerebral leukoencephalopathy and systemic manifestations (RVCL-S), and (Dutch-type) cerebral amyloid angiopathy (CAA). The more prevalent subtypes of migraine with and without (non-motor) aura show polygenic complex inheritance, likely caused by accumulation of common genetic variants with low effect size, and/or rare variants with larger effect size. Increased familial occurrence of migraine as a proxy for genetic load is associated with characteristics such as aura symptoms and lower age-at-onset. In genome-wide association studies ≈40 risk loci have been identified for migraine. While polygenic risk score analyses suggest contribution of common polygenic variation to the familial aggregation of migraine, only a small percentage of inheritance is explained by this variation and a polygenic risk score cannot be used to diagnose migraine in an individual patient. Latent class analyses have to date also failed to associate genetic variants to (clusters of) migraine symptoms. Still, with increasingly larger genetic studies, genetic testing may be used for diagnostic purposes in the future, or, in the light of personalized medicine, aid in identifying migraine patients more likely to respond to acute or prophylactic treatments.
Disclosure: Nothing to disclose.

FW14-3

Diagnostic biomarkers for migraine

P. Irimia
Pamplona, Spain

Abstract: Migraine is an underdiagnosed and undertreated condition worldwide, not least because the early diagnosis of this condition is based on the characteristics of headache and because the clinical phenotypes of migraine patients are extremely variable. The identification of potential biomarkers of migraine will not only help to reduce the subjective nature of migraine diagnosis but also, it will help advance our understanding of migraine pathophysiology. Furthermore, biomarkers would make possible to personalize migraine treatment and predict the risk of progression to a chronic form, which would lead to greater therapeutic success with the consequent social and health benefit. Several circulating molecules have been proposed as diagnostic biomarkers for migraine, including calcitonin gene related peptide (CGRP) and Pituitary adenylate cyclase-activating peptide (PACAP). Recent investigations have identified amylin as a potential biomarker. However, biomarkers for the diagnosis of migraine are not available for routine clinical practice and their role as biomarkers with prognostic value has not been established. Future research may identify novel migraine biomarkers and open new avenues for the development of additional treatment options for patients with migraine. Throughout this presentation, a review on the potential diagnostic circulating biomarkers associated with migraine will be presented.
Disclosure: Pablo Irimia has received honoraria from Allergan, Novartis, Lilly and Teva Pharmaceuticals as a consultant and speaker.

A path toward precision medicine in neurogenetics. One technique for one disease?

FW15-1

Potential of gene editing for neurological diseases

N. Déglon
Lausanne, Switzerland

Abstract: Genome editing is a technology that allows specific modifications of an endogenous loci. Genome editing includes not only the insertion, deletion or replacement of nucleotides, but also the modulation of gene expression and epigenetic editing. Emerging technologies based on ZFs, TALEs, and CRISPR/Cas systems have extended the boundaries of genome manipulation and promoted genome editing approaches to the level of promising strategies for counteracting genetic diseases. The parallel development of efficient delivery systems has also increased our access to the CNS. In this presentation, I will describe the various tools available for genome editing and summarize in vivo preclinical studies of CNS genome editing and illustrate the potential with our recent data on Huntington's disease.

Disclosure:
Nothing to disclose.

FW15-2

Antisense-oligonucleotide

F. Bennett
California, United States of America

FW15-3

Gene Therapy

P. Kaufmann
Washington DC, United States of America

EAN/ECTRIMS The elderly patient with multiple sclerosis

FW16-1

Epidemiology and disease characteristics of late-onset Multiple Sclerosis

M. Magyari
Copenhagen, Denmark

Abstract: Multiple Sclerosis (MS) has primarily been considered a disease of the younger population, though recent scientific reports have shown that the incidence, prevalence, and the mean age at onset of persons with MS are increasing. Late-onset MS , commonly defined as disease onset after the age of 50 years, is considered a rare phenomenon, however, the reported prevalence ranges between 4% and 9.6% in different studies. This may be a result of increased longevity of the general population as well as improved life expectancy in the MS population. Interestingly though, the increase is contributed to both patients with primary progressive (PP) disease course and remitting (RR) disease course, even though PPMS is more frequently seen in the late-onset patient group. It has a female preponderance and its initial presentation is usually monosymptomatic, with a motor or cerebellar symptom. The clinical characteristics and treatment approaches differ from their younger counterparts including an increased rate of reaching disability milestones.
Disclosure: Melinda Magyari has served on scientific advisory board for Biogen, Sanofi, Roche, Novartis, Merck, Abbvie, Alexion has received honoraria for lecturing and research support from Biogen, Merck, Novartis, Sanofi, Genzyme.

FW16-2

Treatment response to disease modifying therapies in elderly MS patients

M. Trojano
Policlinico, Italy

Abstract: Significant advances have been made in the treatment of Multiple Sclerosis (MS), but therapeutic-decision making remain particularly challenging in elderly patients. Most of randomized clinical trials (RCTs) of disease-modifying therapies (DMTs) excluded MS patients older than fifty years. The available efficacy and safety data for those over 50 are subgroup or post-hoc analyses of the pivotal trials, so our knowledge of these treatments in elderly populations is insufficient. Comorbidity, gender, disease activity and higher risk of treatment-related adverse events, including serious infections, represent the major factors influencing the risk-benefit analysis in older patients. Moreover the decision to discontinue DMTs in elderly patients without clinical-radiological signs of inflammatory activity is still a controversial issue. A recent meta-analysis of the main RCTs showed that the efficacy of DMTs on disability worsening is inversely correlated with increasing age, but they suggested the presence of subgroups of older patients that positively responded to the treatments. A multicentre, observational, large cohort study based on prospectively acquired clinical data from the Italian MS Registry, provided evidence that the effectiveness of a sustained exposure to DMTs on risk of disability accumulation, although less significant than in young patients, is still detectable in late onset MS (LOMS) patients. Considering the increasing prevalence of LOMS, further studies specific to this subgroup, using non-traditional markers of disease progression and activity, are both necessary and warranted for identifying subgroups of patients with a favorable benefit to risk balance among LOMS.
Disclosure: MT has served on scientific AB for Biogen, Novartis, Roche, Merck and Genzyme; and she has received research grants for her Institution from Biogen, Merck and Novartis.

FW16-3

Immunosenescence and the risk of disease modifying therapies in Multiple Sclerosis

M. Mehling
Basel, Switzerland

Abstract: During aging, quantitative and functional alterations of immune cells occur and are termed "immunosenescence". While clinically relevant features of immunosenescence occur in most individuals beyond the 6th decade, several conditions have been associated with premature immunosenescence. Examples include chemotherapy, chronic viral infections or autoimmune diseases. Most multiple sclerosis (MS) treatments are regarded as "immunomodulators" rather than immunosuppressants. Despite this, increased vulnerability to restricted sets of pathogens and severe infectious complications can arise in subsets of patients. Except fatalizumab-associated progressive multifocal leukoencephalopathy (PML), the majority of MS patients with infectious complications and particularly PML is older than 45 years. Therefore, age appears as a risk factor for infectious complications under some immunotherapies. Current studies are assessing whether factors such as treatment duration and sequential therapies impact on the development of premature immunosenescence.
Disclosure: Research grants: Swiss MS Society, Basel University, Novartis Foundation, Merck, Roche, Swiss National Science Foundation; Consultancy/honoraria: Actelion, Biogen, Genzyme, Merck, Novartis, Roche (all exclusively used for research support).

EAN/MDS-ES Precision medicine in Parkinson's disease

FW17-1

Precision Medicine for Parkinson's Disease

O. Bandmann
Sheffield, United Kingdom

Abstract: Parkinson's disease (PD) continues to be a relentlessly progressive disorder. The failure of previous clinical trials investigating putative neuroprotective compounds for PD may be due to differences in the underlying pathogenic mechanisms between patients. Genetic stratification may be a particularly promising approach for certain subtypes of PD. However, genetic stratification is unlikely to be applicable to the majority of PD patients in the UK and elsewhere. Doubts whether genetic stratification of common disorders will fulfil the promise of precision medicine have also been cast in other areas of medicine. Precision medicine focussing on mechanistically anchored disease subgroups may therefore hold greater promise. This talk has the following objectives: 1. To explain different concepts of disease stratification in PD to develop a precision medicine approach for future disease modifying therapy 2. To discuss mitochondrial and lysosomal dysfunction as key mechanisms in the pathogenesis of sporadic PD. 3. To describe the role of genetic risk factors such as glucocerebrosidase (GBA) mutations for precision medicine-based disease-modifying therapy in PD I will discuss the concept of biomarker-driven homogenous subtypes of PD likely to respond optimally to therapies proven to affect the causative biological processes within each subtype. I will also provide an update on particularly promising clinical trials for mechanistically defined subtypes of PD.

Disclosure:
Funding from the Medical Research Council (MRC), Michael J Fox Foundation (MJFF), Cure Parkinson's UK (CPT) and the JP Moulton Charity Trust. Trial support from PRO.MED.CS.

FW17-2

Device Aided Therapies for Movement Disorders

R. Katzenschlager
Vienna, Austria

Abstract: The term device-aided treatments is used for deep brain stimulation (DBS) and for infusion therapies that deliver dopaminergic medication in a continuous manner to patients with Parkinson´s disease (PD) . They have an important role in the symptomatic treatment of motor fluctuations that are no longer well controlled on oral treatments. The infusion therapies comprise intestinal levodopa/carbidopa gel, intestinal levodopa/carbidopa/entacapone, and subcutaneous apomorphine, which may all be used during the waking day or around the clock. Levodopa and apomorphine have high level evidence of efficacy and safety. Along with a reduction in daily OFF time, non-motor symptoms and dyskinesia may also improve. In addition, DBS may improve parkinsonian tremor to a greater degree than levodopa. In movement disorders other than PD, DBS has a particular role in some types of dystonia and tremor. Device-aided treatments in PD should be considered for patients as soon as motor complications become difficult to manage orally and all are currently underused in clinical practice.

Disclosure: Regina Katzenschlager has received research funding from Britannia, Stada and Zambon and honoraria for consulting or speaking from AbbVie, AOP Orphan, Bial, Britannia, Ever Pharma, UCB and Zambon.

FW17-3

Update on Developments in Digital Devices for Monitoring of Movement Disorders

A. Sanchez-Ferro
Mostoles, Spain

Abstract: A plethora of new developments are revolutionizing the care of Movement Disorders. Sensors, artificial intelligence, machine learning, ecologically valid, personalized, or precision medicine, are terms that every neurologist should be familiar with. In this session, we will review all these concepts as well as the application in the real life of several of these systems. Digital devices are not the future. Many of these systems are presently available in Europe for improving the management of Movement Disorders patients. In addition to what is ready now, we will also discuss other R&D initiatives that will likely end up translating to the routine practice and disrupt the way we do medicine. After this session, every attendee will obtain a basic understanding of the new digital devices that are available for practice, also their applications, be capable of interpreting the information they provide and also understand what is going to be the next developments that will come.

Disclosure: Patent US 2020/0060622 Al licensed to nQMedical and US 2019/0139221 licensed to Leuko Labs Inc. Stock & salary in Leuko Labs Inc. Honoraria from Abbvie, Bayer, Novartis, PD Monitor, Roche, SEN, Teva, Zambon.

The pearls and pitfalls of neuroimaging for the spinal cord: from diagnosis to treatment

FW18-1

Imaging anatomy: neuroradiological approach

M. Muto
Naples, Italy

Abstract: The spine is a peculiar structure derived from different embryological tissues forming axial skeleton, intra-dural space, spinal cord and peripheral nerves. Due to the anatomical complexity, spinal pathology represents a border country between different medical sub-specialties, generally requiring a close cooperation between neuroimagers, neurologists, neurosurgeons, interventional neuro-radiologists and orthopedic surgeons. From a clinical point of view, signs and symptoms referred to the spine represent one of the most common reasons for medical consultation; although generally related to minor and self-limiting conditions, they can also underpin more complex disorders. Spinal imaging thus represents an essential step in providing robust information for either diagnostic assessment or decision-making support required, in order to offer the most effective tailored therapeutic approach. Therefore a deep knowledge of both anatomy and technology involved in spine imaging is mandatory to improve diagnostic accuracy and to optimize patients' management. Aim of this commentary is to provide a comprehensive overview of cervical, dorsal and lumbar spine anatomy, also focusing on spinal development and normal variants that could mimic pathology of spinal cord and vascular spine structure. Secondly we discuss the use of different spinal imaging modalities in order to improve the mastery of basic skills, also illustrating the role for cutting-edge advanced techniques that could be implemented in routinely clinical practice.
Disclosure: Nothing to disclose.

FW18-2

Infectious and inflammatory diseases

A. Rovira
Barcelona, Spain

Abstract: Neuroimaging studies play an important role in the diagnosis of spinal cord infectious and inflammatory disorders. In particular, MR imaging is the only imaging technique able to directly visualize the spinal cord, and therefore is considered the first imaging modality to be used in the diagnostic work up of patients with suspected inflammatory-infectious conditions involving the spinal cord. However, MR imaging findings are not disease-specific and an accurate diagnosis requires not only a detailed analysis of the extension and topography of the spinal cord lesions, but also of the additional imaging findings that may affect the spinal column and the brain, together with relevant demographic, clinical and laboratory data. A special area of interest is the value of spinal cord MRI in discriminating among different demyelinating disorders such as multiple sclerosis and AQP4 antibody and MOG-antibody diseases, which could be quite challenging in some patients. Also, of crucial clinical relevance is the distinction between inflammatory and vascular spinal cord lesions, being relatively frequent to overdiagnoses demyelinating lesions in ischemic related lesions. In this presentation we will discuss some imaging features that help in establishing an accurate diagnosis of spinal cord inflammatory lesions, and the value of different MR imaging techniques that could add value to this objective.
Disclosure: A. Rovira serves on scientific advisory boards/received speaker honoraria from Novartis, Sanofi-Genzyme, Synthetic MR, Roche, Biogen, and OLEA Medical, Merck-Serono and Teva Pharmaceutical Industries Ltd, Novartis.

FW18-3

Vascular disorders

M. Thurnher
Vienna, Austria

Will precision medicine life-changing for people living with neuromuscular disease?

FW19-1

The role of early genetic diagnostic in the management of patients living with NMDs

T. Evangelista
Paris, France

FW19-2

Digital health technologies in the diagnosis of NMDs

J. Diaz Manera
New Castle, United Kingdom

Abstract: The diagnosis of neuromuscular diseases is a complicated task requiring the combination of clinical data with results of complementary tests. The number of neuromuscular diseases with a genetic diagnosis is increasing progressively and this requires a high degree of specialization to interpret the data obtained from patients and provide a diagnosis. In this regard, artificial intelligence tools that could help clinicians guiding the diagnosis are desiderable. In recent years some studies have applied machine learning strategies to muscle MRI and muscle biopsy to improve their analysis. In this talk I will summarize their main results, discuss potential hurdles that need to be overcome and suggest potential new areas for study

Disclosure: Nothing to disclose.

FW19-3

Robotic rehabilitation in neuromuscular disorders

G. Siciliano
Pisa, Italy

Abstract: A better understanding of the neuromuscular substrates that underlie motor recovery after neurological impairments has led to the development of innovative rehabilitation strategies and tools that incorporate key elements of motor skill re-learning such as intensive motor training involving goal-oriented repeated movements. A robust background of neurophysiological insights is necessary to categorize an impaired neuromuscular system respect to normal conditions, in order to set up robotic devices which elaborate and offset adaptive strategies tailored on single patients in different stages of the disease, with the final purpose to replace the function loss and, when possible, to train it. The effects of combined approaches that target muscle function (e.g., functional electrical stimulation), modulate neuromuscular activity (non-invasive nerve stimulation) and enhance motivation (Virtual Reality) to enhance the benefits of robot-assisted training are only at its initial stage in neuromuscular diseases. A wide range of technologies (including wearable sensors, IMUs and robotics) are available today to make physical activities and rehabilitation treatments more enjoyable and performing for personalized training programmes. Technologies can also provide new tools to include persons with disabilities in many athletic activities and can contribute to the development of novel and very effective rehabilitation procedures that make recovery after injury/disease faster and more effective. In this presentation, the above issues will be discussed with an overview of the status of robot-assisted therapies and combined treatments together with an analysis of the rationale behind them. Finally, the clinical and bioengineering challenges of the next decade will be designed.

Disclosure: CSL Behring, Biogen, Sanofi, Novartis: compensations for lectures and advisory boards.

EAN/EPNS Neurometabolic diseases of childhood growing into adulthood: phenotypes, diagnostic tools and treatments

FW20-1

Treatable Neurometabolic Diseases

B. Plecko
Graz, Austria

FW20-2

Lysosomal Storage Diseases: new treatments and related issues

A. Simonati
Verona, Italy

Abstract: Lysosomal Storage Diseases (LSD) form a large group of multi-organ disorders, most of them with CNS involvement. They are named after the endolysosomal storage of undegraded material leading to cell toxicity and/or death. They are associated with defective lysosomal enzymes; storage can occur related to mutations in genes not coding for lysosomal proteins. Several childhood onset LSD have an early fatal outcome, some present a slow disease progression into adulthood. Rare adult-onset phenotypes can occur. Prolonged survival into second and third decade of severe, early onset LSD results from improved palliative care and management. Early diagnosis is mandatory to start the most appropriate therapies. Replacement Therapy (RT) of defective lysosomal enzymes have become available for few LSD, even with CNS involvement. In some patients dramatic improvement is observed (eg infantile Pompe disease), in others the long term efficacy of RT is still under scrutiny (eg CLN2 disease), in others it has entered the clinical practice (eg Fabry disease). Clinical changes related to the effects of available drugs may result in new phenotypes. Treatments are still lacking for those LSD unrelated to defective lysosomal proteins (eg several NCLs). Still open issue is the opportunity to treat adult-onset patients. Transfer into clinical trials of gene therapies is at dawn. Improved quality of care and effects from new drugs of childhood onset LSD are leading to changes in the pace of disease progression, prolonged survival and require careful monitoring of these conditions by expert neurologists. Appropriate transition-into-adulthood programs for LSD patients are necessary.
Disclosure: Nothing to disclose.

FW20-3

Diagnostic Tools in Neurometabolic Diseases: a Multifaceted Approach

N. Wolf
Amsterdam, The Netherlands

Abstract: Neurometabolic disorders may present a challenge for diagnosis as the individual conditions are rare. Still, as a group, they are relatively common. Because presentations are so diverse, there is not one single way to diagnose a neurometabolic disease: a patient with episodes of rhabdomyolysis needs another set of tests than a patient with a leukodystrophy. Many neurometabolic disorders present in childhood. Adult neurologists see two groups of patients with suspected neurometabolic disorders, patients with disease onset in childhood, but no diagnosis, and patients with disease onset in adulthood. Diagnostic steps need to be tailored to presentation, but also to results of previous investigations. Diagnostic possibilities have been changing for several years now. It is not uncommon that, instead of meticulous metabolic testing, nonselective genetic testing comes first. Sometimes, this leads to a diagnosis quickly confirmed by appropriate metabolic investigations, but it is also possible that variants of yet unknown significance are found with equally ambiguous results at metabolic testing. These cases need an expert approach, ideally in a multidisciplinary setting of neurologists, clinical and laboratory specialists of inherited metabolic disorders and geneticists.
Disclosure: Participation in a clinical trial (Takeda), consultant for Takeda, Ionis, Vigil Neuro and PassageBio, all without personal payment.

Topical Symposia

Saturday, June 19 2021
Targeting CGRP for migraine prevention. What is new?

SYMPTOP01_1

Migraine prevention targeting CGRP. New evidence on efficacy and safety

Z. Katsarava
Essen, Germany

SYMPTOP01_2

A comparison of monoclonal antibodies targeting the CGRP pathway

D. Mitsikostas
Athens, Greece

Monoclonal antibodies targeting the calcitonin gene-related peptide pathway (anti-CGRP mAbs) have shown promising efficacy in randomised clinical trials (RCTs) for the prevention of episodic and chronic migraine (EM and CM), but no head-to-head comparisons with standard treatments are available so far, nor is it desirable necessarily. To fulfil the need for decision making indirect comparisons across pivotal RCTs is need. In this context, to examine absolute differences in benefit-risk ratios between anti-CGRP mAbs, topiramate and propranolol for the prevention of episodic migraine and between anti-CGRP mAbs, topiramate and onabotulinumtoxinA for the prevention of chronic migraine using a likeli-hood to help versus harm analysis may be useful. To perform this analysis the number of patients needed to be treated for a patient to achieve a more than 50% reduction in migraine days (NNTB) was used as an effect size metric of efficacy. The number of patients needed to be treated for a patient to experience an adverse event that led to treatment discontinuation (NNTH) was used as a measure of risk. Likelihood to help versus harm values – which are the ratios of NNTH:NNTB – were calculated using data from phase three randomised clinical trials. By using this analysis, all agents tested were more likely to be beneficial than harmful (likelihood to help versus harm >1) with the exception of topiramate at 200mg per day for the prevention of episodic migraine. Anti-CGRP mAbs in all tested doses had higher LHH values than propranolol or topiramate for EM and onabotulinumtoxinA or topiramate for CM prevention. It seems therefore, that all anti-CGRP mAbs exhibit a more favourable benefit-risk ratio than standard treatments for episodic and chronic migraine. Eventually, head-to-head studies and real-world data and experience are needed to confirm these results. Mean time however, this analysis may help practitioners and health policy makers in decision making.

Disclosure: Nothing to disclose.

SYMPTOP01_3

Individualizing preventive treatment in clinical practice: combination therapy and switching between CGRP antibodies

P. Irimia
Pamplona, Spain

The selection of preventive treatment in patients with migraine is made taking into account the safety and efficacy of the drugs, but also the preferences and comorbidities of the patients. At present, we have different monoclonal antibodies against CGRP or its receptor for the prevention of migraine. Although all antibodies have a common mechanism of action, there are differences between them in relation mainly to the route and periodicity of administration and different side-effects profile. Based on these differences, the clinician must choose which is the most appropriate for each patient. Furthermore, it has been observed that ineffectiveness against one of the CGRP monoclonal antibodies does not necessarily imply that the patient cannot respond to another. Some reports suggest that changing the monoclonal antibody when the response is insufficient or unsatisfactory can improve a significant percentage of patients. On the other hand, clinical experience on the use of monoclonal antibodies against CGRP or its receptor combined with other preventive drugs is growing. Throughout this presentation, news about the preventive treatment of migraine in clinical practice will be presented, specifically addressing the combination therapy and the switch between CGRP monoclonal antibodies.

Disclosure: Pablo Irimia has received honoraria from Allergan, Novartis, Lilly and Teva Pharmaceuticals as a consultant and speaker.

Monday, June 21 2021

Assessment and burden of treatment in Myasthenia Gravis; from new antibodies to emerging therapies

SYMPTOP03_1

Old and new myasthenia gravis antibodies: what is our current phenotype understanding?

C. Schneider-Gold
Berlin, Germany

MG is a prototypic auto-immune disease with pathogenic antibodies (abs) directed against distinct antigens of the neuromuscular endplate including acetylcholine receptor (AChR), muscle specific tyrosine kinase (MuSK) and lowdensity lipoprotein related receptor protein 4 (LRP4). Abs to agrin, collQ-, cortactin, Kv1.4. and RyR are of unknown significance and not related to a distinct type of MG. The different types of pathogenic antibodies act differently at the neuromuscular endplate and determine different types of immunopathology and response to treatment. AChR-abs belong to IgG subclasses IgG 1, IgG2 or IgG3 and may activate complement leading to destruction of neuromuscular endplate structures by the membrane attack complex (MAC). MuSK abs are IgG4 abs and act by direct disruption of the interaction of LRP4 with MuSK which is required for the clustering of the AChR, but can also disperse preformed agrin-independent AChR clusters. IgG4 is not able to activate complement. Anti-MuSK abs are thought to be produced by short-lived plasma blasts which is in accord with the better response to rituximab in MuSK-ab positive than in AChR-ab positive MG in several studies. LRP4 abs were shown to belong to the complement activating IgG1 subtype and to be able to disrupt agrin-LRP4 signalling. With regard to the upcoming new therapeutic agents in MG the determination of ab IgG-subclass type has gained increasing relevance/implications for treatment strategies.

Disclosure: Nothing to disclose.

SYMPTOP03_2

Electrophysiological standards for the diagnostics of myasthenic syndroms

A. Kostera-Pruszcyk
Warsaw, Poland

SYMPTOP03_3

Congenital myasthenic syndrome of the adulthood

J. Palace
Oxford, United Kingdom

SYMPTOP03_4

Current and emerging therapies: what comes next?

C. Rodolico
Messina, Italy

Myasthenia gravis (MG) is a chronic disorder of the neuromuscular junction characterized by a complex impairment of the immune system. The long-term effects of classic immunosuppressants, including steroids, constitute a limit that must hopefully be overcome; furthermore many patients are resistant to this conventional treatment and effective and safe therapies are needed. New molecules targeting compounds of the immune system as B cells, pro-inflammatory cytokines and their receptors, complement, Fc neonatal receptor (FcRn) have been recently developed. Rituximab, a monoclonal antibody directed against CD20 antigen on B cells, is successfully employed in patients with antibodies against muscle-specific kinase (MuSK). Contrasting data have been reported in the literature concerning the benefit of indirect B cells targeting agents, such as etanercept, infliximab, belimumab and bortezemib. The benefit of complement inhibitors has been proved in MG linked to IgG1 antibodies against acetylcholine receptor (AChR). Neonatal Fc receptor antagonists, including efgartigimod and rozanolixizumab, which reduce IgG plasma levels, blocking their recycling and increasing their clearance could be a promising therapeutic option in all forms of MG. Nevertheless, high cost, potential adverse events during chronic therapy, and production of anti-drug antibodies, could be some limitations of these new biologics which deserve to be considered.

Disclosure: Nothing to disclose.

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Special Sessions

Saturday, June 19 2021

EAN COVID-19 Special Session – what did we learn from the pandemic for patient care

SPS01-1

Impact of COVID-19 on people with chronic neurological disease

A. Sauerbier
Cologne, Germany

SPS01-2

The patient's perspective: analysis of the EFNA survey

D. Walsh
Brussels, Belgium

Many surveys have captured the impact of the Covid-19 pandemic on patients' access to treatment and care. However, a survey by the European Federation of Neurological Associations [EFNA] – in partnership with EAN – aimed to better understand how care pathways were reconfigured for the neurology patient community during the pandemic. However, more importantly, they survey captured recommendations to ensure that any future changes to service delivery are made in the interests of the patients – rather than, solely, in the interests of the healthcare system. This presentation will present the results and conclusions of this survey, as well as combining these with the disease specific concerns of our community. The presentation will present recommendations to inform future advocacy around the recovery planning process. It will also allow neurologists across Europe to understand the views of their patients to the approaches adopted during the pandemic, but also which learnings can be applied in the future delivery of care.

Disclosure: EFNA receives funding from a consortia of pharmaceutical companies annually to support its work programme. See companies and details of financial support: https://www.efna.net/about-us/finance-funding/

SPS01-3

Disruption of neurological patient care

M. Zedde
Reggio Emilia, Italy

The COVID-19 pandemic caused unprecedented stress on the organization of health systems and led to a sudden disintegration of the usual pathways for the management of diseases and in particular of neurological ones. These considerations are equally valid for the management pathways of the acute phase of time-dependent pathologies, such as stroke, and for those of chronic neurological diseases. During the first pandemic wave, in which health systems were totally unprepared to face the situation, it was also necessary to face the management of acute neurological conditions in patients with COVID-19 and in particular of the neurological manifestations of COVID-19. Territorial and hospital resources have been largely dedicated to the management of patients with COVID-19 and very few other time-dependent diseases, while chronic neurological diseases have seen the previous follow-up management totally suspended in some cases. Add to this the fear of the population in accessing a place that has transformed from a place of care into a place of greater risk of contracting COVID-19, with reduction and delays in access even for treatable diseases, like the stroke. Add to this the fact that many health workers have been affected by COVID-19, leaving the usual treatment path even more unguarded.

Disclosure: Nothing to disclose.

SPS01-4

Neurological side effects of SARS-CoV-2 vaccination

E. Moro
Grenoble, France

SPS01-5

Impact of COVID-19 pandemic on neurology residents and research fellows in Europe

G. Di Liberto
Lausanne, Switzerland

COVID-19 pandemic is profoundly affecting healthcare workers and disrupting numerous residency programme and research activities. Neurology residents and research fellows are profoundly contributing to the functioning of the healthcare system and academia and therefore exposed to already numerous factors participating to an increased risk of burnout. The Resident and Research Fellow Section (RRFS) of the European Academy of Neurology (EAN) has decided to assess the impact of the COVID-19 pandemic on neurology training as well as its consequences on burnout rates of neurology residents and researchers in Europe taking advantage of two surveys. Seventy-nine per cent of

the respondents (n=222) of the neurology training survey felt that the pandemic will probably have a serious impact on their training and career, given the numerous adaptations and limitations affecting their daily practice. Among the responders (n=358), the burnout survey revealed that roughly, one third of neurology residents and researchers fulfilled the criteria for burnout, while pathological scores in at least one burnout dimension characterized another third of the responders. However, burnout profiles were not significantly influenced by the ongoing pandemic but rather other factors such as job satisfaction, social support and work-related fatigue. Our surveys shed light on the workplace well-being of neurology residents and research fellows in Europe highlighting potential factors contributing to their work-related distress, thus opening up novel strategies to mitigate them in the future.

Disclosure: Nothing to disclose.

EAN/MDS-ES European Basal Ganglia Club

SPS02-1

C. David Marsden Award Lecture: Cognition and Movement

E. Ruzicka
Prague, Czech Republic

Neuro-Covid across the continents

SPS03-1

Epidemiology is different but the course of the disease is similar

M. Abd El-Naseer
Cairo, Egypt

Novel coronavirus is a new virus that has not been previously identified. This virus is causing coronavirus disease 2019 (COVID-19) which is a new disease that has not previously been seen in humans. In March 2020, the WHO declared the novel coronavirus outbreak a pandemic. COVID-19 is primarily a respiratory disease and most infected people will develop mild to moderate symptoms and recover without requiring special treatment. Common symptoms include: Fever, Tiredness, Dry cough. Other symptoms include: Shortness of breath, Aches and pains, Sore throat, Diarrhea, nausea or a runny nose. The human nervous system emerges as a new target of the Coronavirus. Patients with COVID-19 have been reported with mild (anosmia and ageusia) to severe (encephalopathy) neurological manifestations. There is evidence from the animal experiments in mice that coronavirus enters the brain through a retrograde transfer via the olfactory epithelium or through the cribriform bone and reaches the brain in seven days' time. Secondly, during the viremia phase of illness, disruption of blood brain barrier causes the virus to enter the brain directly. Another postulated mechanism is the invasion of peripheral nerve terminals by the virus which then gains entry to the CNS through the synapse connected route. The Middle East and north africa region (MENA) witnessed a rapid rise in the number of confirmed cases with Iran emerging as its epicenter. In addition, Egypt faced a rapid surge in the number of infections and deaths.

Disclosure: Received honoraria as Speaker for Novartis, Roche, Merck, Sanofi-Genzyme, Bayer, Served on advisory boards of Merck, Novartis, Roche, Sanofi-Genzyme, Lilly

SPS03-2

The central and peripheral nervous system manifestations of COVID-19: pathogenic mechanisms

R. Du Pasquier
Lausanne, Switzerland

The neurological complications of COVID-19 are subjected to intense debates. Here, I will first briefly review the different neurological manifestations of SARS-CoV-2. Those affecting the central nervous system are: intensive care unit-related encephalopathy or delirium, stroke, and encephalitis. The complication affecting the peripheral nervous system is essentially the Guillain-Barré syndrome. For each of these complications, some controversies exist: is the post-ICU encephalopathy specific to COVID-19 or is not just due to a long stay in the ICU? Is anosmia a neurological or an ENT complication? What is the mechanism underlying the encephalitis presented by some patients: directly infectious or due to a dysregulated immune response? After having discussed the underlying mechanisms of these different conditions, I will address the controversial question of long-term neuro-cognitive sequelae of COVID-19.

Disclosure: Nothing to disclose.

SPS03-3

Managing the Covid pandemic in sub-Saharan Africa: The South Africa experience

L. Tucker
Cape Town, South Africa

Precision Medicine and Rare neurological disorders

SPS04-1

Genotype-phenotype relationship in neuromuscular diseases (challenges and opportunities)

V. Straub
Newcastle, United Kingdom

SPS04-2

Novel molecular strategies to solve ultra-rare diseases (The Solve-RD Project)

H. Graessner
Tübingen, Germany

SPS04-3

Personalized Treatments in rare neurologic diseases

H. Kearney
Dublin, Ireland

Precision medicine is a concept that has been informally engrained in medical practice since inception. However, more recently a formalised or more proscriptive method of practicing precision medicine has emerged, and to the forefront of this has been a significant advance in genomics. Whilst genetic sequencing has had distinct advantages for a range of medical specialties, in neurology it now forms part of the routine clinical armamentarium, and importantly has therapeutic implications. In the case of precision medicine in neurology the epilepsies have been a bellwether in this regard, and whilst each individual monogenic epilepsy might be rare, precise diagnostics and treatment can have significant implications for care of the individual.
Disclosure: Speaking honoraria from Biogen, Roche, Teva and Novartis

SPS04-4

Clinical and Imaging biomarkers in X-linked adrenoleukodystrophy

M. Engelen
Amsterdam, The Netherlands

More than a gut feeling: The gut brain axis in neuroinflammation and neurodegeneration

SPS05-1

Why the gut-brain axis is important for precision neurology – the neuroscientist's view

S. Vascellari
Cagliari, Italy

SPS05-2

The gut-brain axis in multiple sclerosis and neuroinflammation: pathophysiology and targets for therapy

H. Wekerle
Munich, Germany

SPS05-3

Does gut microbiota play a role in neurodegenerative disorders?

F. Scheperjans
Helsinki, Finland

Spearheaded by initial encouraging findings in Parkinson's disease, research interest in the links between the gut microbiota and neurodegenerative disease has grown exponentially in recent years. Gut microbiota influence brain health and physiology through multiple mechanisms including the immune system, vagus nerve, metabolites, and neurotransmitters. With respect to neurodegeneration, also potential effects on protein aggregation have been reported. This talk will give an overview on the current state of microbiota research with a focus on Parkinson's and Alzheimer's disease and other neurodegenerative disorders. The impact of microbiota on disease risk, progression, symptoms, and therapy will be discussed.

Disclosure: Stocks in NeuroInnovation Oy and NeuroBiome Ltd.. Consulting fees and stock options: Axial Biotherapeutics. Consulting and lecture fees: Abbvie, Herantis, Orion, GE Healthcare, Merck, Teva.

SPS05-4

Is there a role for the gut-brain axis in the pathophysiology and treatment of epilepsy?

K. De Looze
Ghent, Belgium

The gut microbiota, a complex ecosystem of micro-organisms present in the gastrointestinal tract, are increasingly suggested as potential key players in several neurological disorders. Recently, the concept of the microbiota-gut-brain axis has begun to find its way into epilepsy research. The gut microbiota are involved in host immunity, inflammation, barrier integrity and host signalling, all processes undeniable linked with epileptogenesis. This lecture will consist of a brief overview of current literature on the overlapping pathways between the gut microbiota and epilepsy as well as microbiota-based interventions in epilepsy treatment and how this could translate into future research.

Disclosure: Nothing to disclose.

Sunday, June 20 2021
New neurological guidelines

SPS06-1

Establishing criteria for prioritization of topics for EAN Clinical practice guidelines.

K. Aleksovska
Skopje, Macedonia

Over the last years, there has been an increase in the EAN guideline production and the number of received proposals. To direct resources towards the most needed guidelines, while contributing to achieving transparency, equity, and accountability, the EAN is conducting a project of developing a systematic procedure for prioritisation of topics for Clinical Practice Guidelines. For this purpose, the EAN Guideline Production Group (GPG) organized a Delphi consensus process among the persons involved in the production of guidelines, including GPG, EAN Scientific Committee members, Co-chairs and RRFS and patient representatives from each Scientific Panel, National representatives from the Assembly of Delegates, and policy makers from international organizations. The aim of this consensus is to define criteria for prioritization of EAN guideline topics. During the first Delphi phase, participants are asked to vote on the importance of several prioritization criteria, used by other organizations, using a 1–9 Likert scale. They are allowed to propose additional criteria. Criteria that will be voted as 7–9 (high importance) by >70% of the participants will be included, and those voted as 1–3 (low importance) by >70% will be excluded. A discussion is encouraged by asking the participants to add rationale behind their choices. The second Delphi round will contain the proposed criteria, the criteria that didn't reach the threshold of inclusion or exclusion, and additional questions regarding the process of their implementation. The whole Delphi procedure is planned to be conducted in a two-months period, and the results will be presented during the EAN-2021 congress.

Disclosure: Nothing to disclose.

SPS06-2

EAN guidelines on the treatment of cluster headache and other trigeminal-autonomic cephalalgias (TAC)

R. Hojland Jensen
Glostrup, Denmark

Background: Trigeminal-autonomic cephalalgias (TACs) are relatively rare, but very disabling primary headache disorders with a major impact on the patients' quality of life.

Objectives: To present evidence-based recommendations for the treatment of TACs derived from a systematic review of the literature and consensus among a panel of experts.

Methods: The databases PubMed (Medline), Science Citation Index, and the Cochrane Library were screened for studies on the effectiveness of interventions for cluster headache, paroxysmal hemicrania, hemicrania continua, SUNA syndrome and SUNCT syndrome. The findings in these studies were evaluated according to the recommendations of the European Academy of Neurology and the level of evidence was established using Grading of Recommendations Assessment, Development and Evaluation (GRADE). For cluster headache recommendations were principally based on controlled trials, while recommendations for other TACs include evidence from case-studies and case-series.

Recommendations: A detailed list of recommendations for the acute and preventive treatment of cluster headache are recommended. Nerve stimulation is also used but there is limited evidence for its effectiveness. There is a strong recommendation for paroxysmal hemicrania for indomethacin but otherwise only weak recommendations for the remaining TAC's. The guideline recommendations will be presented and discussed.

Disclosure: RHJ is or has been principal investigator in studies sponsored by Lundbeck, Eli Lilly and ATI and has given lectures for Novartis, Lundbeck, Allergan, TEVA and ATI.

SPS06-3

EAN-PNS Guideline on Guillain Barré Syndrome (GBS)

P. Van Doorn
Rotterdam, The Netherlands

SPS06-4

EAN-PNS Guideline on diagnosis and management of chronic inflammatory demyelinating polyradiculoneuropathy (CIDP)

P. Van den Bergh
Brussels, Belgium

The 2010 guideline on management of chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) needed to be revised. A Task Force (TF) of 20 experts from 11 countries worldwide, including a patient representative and two methodologists constructed 12 PICO (Population/Intervention/Comparison/Outcome) questions. Data were summarized in GRADE (Grading of Recommendations Assessment, Development and Evaluation) evidence profiles (treatment) or evidence tables (diagnosis). Statements were prepared according to Evidence-to-Decision (EtD) frameworks. The TF received unrestricted grants from the EAN, PNS, GBS/CIDP Foundation International, and the UK GAIN Charity for the guideline project. The TF distinguished typical CIDP and CIDP variants. The previously used term 'atypical CIDP' was replaced by 'CIDP variants'. These variants, multifocal, focal, distal, motor, or sensory CIDP, are well characterized entities with specific clinical and electrodiagnostic phenotypes. Because there is insufficient distinction between criteria for probable and definite CIDP without a gold standard for CIDP diagnosis, the TF reduced the levels of diagnostic certainty from three (definite, probable, possible CIDP) to only two: CIDP and possible CIDP. The TF agreed on Good Practice Points (GPP) to define clinical, electrodiagnostic, and supportive criteria and investigations to be considered to diagnose CIDP. The principal treatment recommendations are: (a) IVIg or corticosteroids are strongly recommended in typical CIDP and CIDP variants; (b) if IVIg and corticosteroids are ineffective, plasma exchange is strongly recommended; (c) IVIg should be considered as the first-line treatment in motor CIDP (GPP); (d) no preference is recommended for either IVIg or SCIg for maintenance treatment.

Disclosure: Nothing to disclose.

PH.D. and the neurology residency: why, when and how?

SPS08-1

A Ph.D. degree can be done before entering Neurology Training

A. Sauerbier
Cologne, Germany

SPS08-2

A Ph.D. degree can be started during the Neurology Training

D. Aguiar de Sousa
Lisbon, Portugal

Physician–scientists, individuals trained in both clinical practice and scientific research, are particularly well-equipped to address pressing questions in medical research. In parallel with the increasing development of clinical research in Neurology in the last decades, the need to improve the early research training of physicians has also expanded globally. However, although several Institutions in Europe are offering special pathways to doctoral degrees in Neurology that can be combined with residency curricula, many young physicians are still faced with doubts and difficulties on how to combine two such demanding programmes. In this lecture we will discuss some of the challenges and advantages of starting doctoral level programmes during residency, including issues such as access to research training, funding, length of training and protected research time. Examples of physician–scientist track residencies will be compared. We hope this talk can help trainees considering this pathway.

Disclosure: Dr Aguiar de Sousa reports nonfinancial support from Boehringer Ingelheim outside of the submitted work.

SPS08-3

A Ph.D. degree can be started after the conclusion of the Neurology training

D. García Azorín
Valladolid, Spain

The duration of neurology residency is heterogeneous across Europe. A shorter duration might difficult an adequate training in disciplines such as research and pre-clinical science. In some countries, like Spain, most doctors start residency immediately after the high school, and the concentrated training in neurology makes difficult dedicating time to the PhD during residency. For these reasons, many neurologists start their PhD projects after the residency completion. If the topic of the PhD project is based on clinical neurology, working as neurologist may facilitate the recruitment and study of patients. Indeed, the sub-specialization in a specific field of neurology can be a great opportunity to acquire the knowledge and competencies of the subspecialty of neurology. There are several transversal competencies that are desirable for every PhD candidate, and indeed, for every neurologist. These include epidemiology, design of research studies, biostatistics, medical writing, critical appraisal to a topic and critical evaluation of manuscripts. In the present lecture, some tips on how to complete the PhD project after the residency of neurology and simultaneously start the first steps as neurologists will be delivered.

Disclosure: DGA declares no conflict of interest related with the present lecture.

SPS08-4

You can have a research career without doing a Ph.D.

L. Klingelhoefer
Dresden, Germany

The neurological training throughout Europe is quite different as investigated by the Resident and Research Fellow Section of the EAN. As so are the different paths of potential research careers. However, the individual development often depends on different factors. Some of these factors can be influenced, e.g. the kind and the topic of research you are interested in but some factors are more difficult to influence or to overcome like your working environment and surrounding structures, financial restrictions, the support you get. I would like to provide an example of my way performing the neurological training in combination with research without doing a Ph.D. I am going to provide you an insight of my personal experience, important factors and possible pitfalls on how to become a clinician-scientist.

Disclosure: Nothing to disclose.

Monday, June 21 2021

Central European contribution to the discovery and naming of major neurodegenerations

SPS09-1

Alois Alzheimer and the group of great reputation

H. Förstl
Munich, Germany

A famous photograph from Emma Wilson Davidson Mooers' and Aloys Alzheimer's laboratory shows a number of significant figures from second generation of scientists in the laboratory and the early days of "Alzheimer Research". Their work would not have been possible without the skillful contributions of Adele Grombach and Karl Gruber. Max Isserlin and several others provided stimulating intellectual input, but the most important studies on neurodegenerative disease was carried out by four experts standing and sitting on Mooers' and Alzheimer's left side: Nicholas Achucarro, Friedrich Lewy, Francesco Bonfiglio and Gaetano Perusini. The presentation will focus on Mooers' and on their work.
Disclosure: Nothing to disclose.

SPS09-2

Arnold Pick, life for neurology and neuropathology

E. Ruzicka
Prague, Czech Republic

SPS09-3

Examined by a neuropathologist – from today's point of view

T. Warner
London, United Kingdom

The neuropathological examination of neurodegenerative diseases, such as Alzheimer's and Parkinson's disease, fronto-temporal dementia and motor neuron disease, has become increasingly complex. The expectation is beyond that of a single diagnosis and now involves detailed staging of the pathology, and the role of dual or multiple pathologies. It incorporates increasingly complex immunohistochemical regimes, use of biochemistry, and molecular genetics to extract the maximum diagnostic information, and relevance for family members of the patient. Understanding the neuropathological effects of aging is important, and pathological effects of deposition of one or more proteins and their subsequent spread in a prion-like fashion have permitted more accurate diagnosis. In addition, the advent of potential disease modifying treatments targeting specific proteins such as tau and alpha-synuclein, have meant subsequent neuropathological examination is crucial.
This talk will use cases from the Queen Square Brain Bank to illustrate how the use of a range of immunohistochemical and molecular genetic investigations are becoming routine for the neuropathological examination to reach an accurate diagnosis. This precision is critical for the families of the patient, as well as being a key resource for research into the underlying mechanisms of neurodegenerative disorders.
Disclosure: Nothing to disclose.

PAUNS – Dementia: a growing interest in the Arab world

SPS10-1

Dementia in Arab world: challenges and new hopes

M. Farghaly
Cairo, Egypt

SPS10-2

Neuropsychiatric manifestations of dementia: pathophysiology and management

H.O. Tayeb
Jeddah, Saudi Arabia

SPS10-3

Genetics and clinical aspects of Dementia with Lewy bodies

M. Den Djebara
Tunis, Tunisia

SPS10-4

Management of AD in Morocco

M. Benabdeljlil
Rabat, Morocco

Tuesday, June 22 2021

AFAN – Neurology training in Africa: future perspectives

SPS11-1

Neurology training in West Africa: Experience of the WFN training centre of Dakar

M. Fall
Dakar, Senegal

SPS11-2

Training the neurologist-researcher: requisites for successful African research

N.F. Rasaholiarison
Fianarantsoa, Madagascar

SPS11-3

Neurology training in the East African region: Experience from Ethiopia

Y.Z. Zewde
Addis Ababa, Ethiopia

SPS11-4

Neuroscience and Neurology in the path of a neurologist

H. Tibar
Rabat, Morocco

WFN Special Session: promoting brain health

SPS12-1

World Federation of Neurology Expanding Role in Education

W. Carroll
Perth, Australia

SPS12-2

WFN Existing Educational Activities

S. Lewis
Pennsylvania, United States of America

The mission of the WFN is to foster quality neurology and brain health worldwide, a goal we seek to achieve by "promoting global neurological education and training, with the emphasis placed firmly on under-resourced parts of the world" (wfneurology.org). With this goal in mind, the WFN created the Regional Training Centre program. The concept of the WFN Training Centres includes leveraging existing high-quality regional neurology training programs that are already in place, to increase the number of well-trained neurologists in regions currently underserved with regard to neurological training and neurological care. The process of Training Centre accreditation includes defining regional needs, inviting applications from existing regional training sites, followed by a site visit. WFN-sponsored trainees are chosen by a diversely-represented team including WFN and regional representation. WFN Training Centres currently include four sites in Africa; two (Mohamed V University in Rabat, Morocco, and Cheikh Anta Diop University in Dakar, Senegal) devoted to training of neurologists from francophone sub-Saharan Africa, and two (Cairo University in Cairo, Egypt, and the Universities of Cape Town and Stellenbosch in Cape Town, South Africa) devoted to training of neurologists from Anglophone sub-Saharan Africa. A site in Mexico is aimed at training Spanish-speaking neurologists from Central and South America. This lecture will include an overview of the concept and development of the WFN Training Centres, and video interviews from recent trainees from both anglophone and francophone centres. Plans for further development and optimization of the program will be discussed.

Disclosure: Dr. Lewis is an Elected Trustee of the WFN and Editor-in-Chief of the journal Continuum: Lifelong Learning in Neurology

SPS12-3

New Activities. The WFN Needs Registry

W. Grisold
Vienna, Austria

The World Federation of Neurology (WFN) is compiling an inventory of the most important deficiencies causing inequalities in the prevention and care of neurological disorders in partnership with its member societies. The WFN Neurological Needs Registry (NR) is a study being executed during 2020–2021 and data collected mainly from WFN Member Societies (122). The WFN NR, identifies and analyses the spectrum of needs for neurological patients. Looking at the distribution of the world population and the large variations of GPD, per capita income he overarching questions are not only access and availability but also affordability. Important and often complex issues are the number neurological services, available diagnostics and therapeutics and the number of neurologists and trained health professionals. The challenges facing neurologists in their countries as well as the most urgent local needs are assessed. The access to medications and drugs is compared with the WHO Model List of Essential Medicines which is a core list of minimum medicines needs for a basic health-care system. It lists the most efficacious, safe and cost–effective medicines. The needs registry of the WFN is an important contribution towards the assessment of neurological needs globally and adds a new views following the two editions of the WHO-WFN Atlas. The identification of the local public neurological needs is a prerequisite and basis for further engaged research projects. These projects aim at the interaction of the scientific community with policy makers, and will beneficial promote neurology.

Disclosure: Nothing to disclose.

SPS12-4

Selected WFN Specialty Group Activities

M. De Visser
Amsterdam, The Netherlands

How sex and gender differences may impact research and clinical practice in neurology

SPS13-1

The impact of sex and gender on the history of global health and care in neurology

S. Bhattacharya
York, England

SPS13-2

Sex-related differences in genetic neurological disorders

C. Klein
Lübeck, Germany

SPS13-3

Impact of sex and gender on clinical presentation, associated factors, research and management of migraine

E. Lebedeva
Yekaterinburg, Russian Federation

Migraine is a neurovascular disorder that affects over one billion people worldwide and occurs in women 3–4 times more often than in men. Migraine is the second leading cause of disability and accounts for more disability than all other neurologic disorders combined, this is a major cause of tremendous losses to the global economy. Migraine is the leading cause of disability worldwide in women younger than 50 years. Women have more severe, longer and frequent attacks leading to greater disability, longer recovery period and tendency to become chronic. Men tending to have longer remission periods than women and attribute lower health state utilities to migraine conditions compared to women. Factors associated with migraine are different in women and men. According to our studies of headache in three different social groups, insomnia (2.7, 95% CI 1.1–6.9), depressed mood (OR 2.1, 95% CI 1.1–4.2), low physical activity (OR 1.9; 95% CI 1.1–3.2) and consumption of light alcoholic beverages (OR 3.49; 2.03–6.02) were associated with migraine in females. To be a student was associated with the highest risk of migraine (OR 6.6; 95% CI 4.2–10.4). Further studies with a primary objective to identify sex- and/or gender differences are necessary across all relevant basic, clinical and population science domains using interdisciplinary approach, more researches should identify the range of indirect consequences of migraine in women and yield a full account of migraine attributed burden in different social groups, to improve health-care policies, clinical practices and health-care strategies.

Disclosure: Nothing to disclose.

SPS13-4

The new perspective in sex and gender-oriented management of neurological disorders

G. Arabia
Catanzaro, Italy

Neurological disorders often require differential diagnostic and therapeutic approaches in male and female patients. Genetic, hormonal, and reproductive factors need to be taken into account when analyzing the risk factor profiles of the neurological patients, but also in planning diagnostic examinations and balancing the risks and benefits of a range of treatments. Tailored therapeutic strategies in women of childbearing age, e.g., affected by epilepsy or multiple sclerosis, are emblematic examples of the impact of sex and gender in the management of some neurological disorders. Furthermore, aging of the general population brings out new epidemiological and socio-economics perspectives on the burden of neurodegenerative disorders, which have a differential impact between men and women. Covid-19 pandemic has also raised a number of different gender issues, spanning from different incidence of risk factors and occurrence of neurological complications to gender inequality in healthcare workforce involvement and risk of stress and burnouts. Another emerging sex- and gender-related aspect of the management of the neurological disorders is related to the differential burden for caregivers. Indeed, the vast majority of caregivers of neurological patients are women and this has a major impact on differential occupational and socio-economic factors. Gender inequality in the management of neurological disorders has to be recognized and analyzed by collecting sex-disaggregated data. There is an urgent need to further evaluate sex and gender issues in health management to design effective policies able to reduce vulnerable neurological conditions in both men and women.

Disclosure: Nothing to disclose.

The European Brain Research Area (EBRA)

SPS14-1

Introduction to the European Brain Council (EBC) and the European Brain Research Area (EBRA)

M. Di Luca
Milano, Italy

SPS14-2

The shared European Brain Research Agenda (SEBRA)

K. Aarts
Brussels, Belgium

In late 2019, the European Brain Council (EBC) launched the development of the Shared European Brain Research Agenda (SEBRA). SEBRA is framed within the European Brain Research Area (EBRA) project, an EU-funded (Horizon 2020) catalysing initiative for brain research stakeholders (researchers, clinicians, patients, governments, funders and public institutions) to streamline and better coordinate brain research across Europe – while fostering global initiatives – with the goal to maximize cooperation and reduce overlap and fragmentation. It brings together four key players in the brain space: the European Brain Council, the ERA-NET NEURON, the EU Joint Programme – Neurodegenerative Disease Research (JPND) and the Human Brain Project (HBP). The aim of SEBRA is to identify research opportunities and research and innovation gaps to be addressed in the field and to provide recommendations on future areas for excellent, innovative and translational brain research in Europe. SEBRA covers all brain research fields and brain disorders, including both psychiatric and neurological disorders and will serve as a framework to guide future brain research investments in Europe. Such a framework allows to: 1. Increase the impact of brain research; 2. Advance basic, translational and clinical brain research; 3. Improve the lives of persons with brain disorders; 4. Enable brain innovation; and 5. Address societal and economic challenges in Europe and globally.

Disclosure: This EBRA project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 825348

SPS14-3

Accelerating coordination of brain research clusters in Europe

F. Destrebecq
Brussels, Belgium

SPS14-4

Round Table: Epicluster, Brainfood, Trisomy21, Premos, Psmd

SPS15

EPA – How your brain can starve you to death: from reward circuitry to anorexia nervosa

SPS17

PAFNS – Tropical Neurology

SPS18

AOAN – Advances in neurological research and Asian-European collaboration

Oral Presentations

Saturday, June 19 2021
Motor Neurone Disease 1

OPR-001

Neural correlates of motor imagery of gait in amyotrophic lateral sclerosis

M. Abidi [1], G. De Marco [1], P. Pradat [1], P. Bede [2]
[1] Paris, France, [2] Dublin, Ireland

Background and aims: Gait impairment is understudied and poorly characterised in Amyotrophic Lateral Sclerosis (ALS), despite increasing evidence of considerable extrapyramidal and cerebellar dysfunction. Gait impairment adds to the considerable motor disability of ALS patients and requires target multidisciplinary interventions. The objective of this study is to assess gait imagery specific-networks and functional adaptation in ALS.
Methods: 17 ALS patients with lower motor neuron predominant (LMNp) disability, fourteen patients with upper motor neurons predominant (UMNp) disease and fourteen healthy controls performed a dual motor imagery task on fMRI; normal and precision. The Movement Imagery Questionnaire – Revised Second Version (MIQ-rs) was used to appraise movement imagery in each participant. Study-group specific activation patterns were evaluated during motor imagery of gait. Additional generalized psychophysiological interaction analyses were carried out using the supplementary motor area, caudate, cerebellum, and superior parietal lobule as seed regions.
Results: Our data revealed a significant increase in imagery time in UMNp patients compared to controls and LMNp during imagined gait. UMNp patients exhibited decreased SMA, DLPFC and superior parietal lobule activation and increased orbitofrontal, parietal and cerebellar signal during imagined locomotion. Increased effective connectivity of the striato and parieto-cerebellar circuits was also demonstrated. Additional activation was detected in the insula and cingulate cortex.
Conclusion: Our results suggest functional reorganisation in ALS. Enhanced striato- and parieto-cerebellar networks in UMNp ALS patients are likely to represent a compensatory response to impaired postural control. Activation of insular and cingulate regions suggest that fear of falling is a an implication of gait disturbance in ALS
Disclosure: All authors have approved the abstract and agree with submission

OPR-002

Impaired recognition of disgust is related to subcortical volume loss in amyotrophic lateral sclerosis

V. Castelnovo [1], E. Canu [1], M. Magno [2], N. Riva [3], B. Poletti [1], V. Silani [4], M. Filippi [5], F. Agosta [1]
[1] Neuroimaging Research Unit, Division of Neuroscience, Milan, Italy, [2] Neuroimaging Research Unit, Institute of Experimental Neurology, Division of Neuroscience, Scientific Institute San Raffaele, Milan, Italy, [3] Department of Neurology and INSPE, Milan, Italy, [4] Department of Neurology and Laboratory of Neuroscience, Milano, Italy, [5] Neurology and Neurorehabilitation Unit, Neuroimaging Research Unit, Neurophysiology Service, Milano, Italy

Background and aims: The impairment in detecting disgust in Amyotrophic Lateral Sclerosis (ALS) has been hypothesized to be related with the integrity of subcortical structures. However, this has not been demonstrated yet and was the aim of the study.
Methods: 20 ALS patients without cognitive/behavioural symptoms and 52 matched healthy controls (HC) underwent a brain MRI scan and a neuropsychological assessment including the Comprehensive Affect Testing System (CATS) investigating emotion recognition. Composite scores were calculated by summing up the correct answers for each emotion. Gray matter (GM) volumes of the subcortical structures were obtained using FIRST in FSL. Sociodemographic, cognitive and MRI data were compared between groups. In ALS patients, CATS significant findings were correlated with the subcortical volumes, ECAS performances, patients' mood and behaviour.
Results: ALS patients performed significantly worse than HC at the CATS, and they were significantly less able to recognize disgust. No GM volume differences were observed between groups. In ALS patients, a low performance in disgust recognition was related with a reduced volume of the left pallidum and with low performances at the ECAS.
Conclusion: In a sample of cognitively/behaviourally unimpaired ALS, we demonstrated an altered ability to correctly recognize disgust and a potential role of basal ganglia in the altered processing of this emotion. These findings, together with the relationship between the altered disgust recognition with lower ECAS performances in patients, suggest that disgust could be the first emotion to be hit in ALS cognitive decline. These findings offer new potential markers for monitoring extra-motor progression in ALS.
Disclosure: Italian Ministry of Health (GR-2013-02357415); European Research Council (StG-2016_714388_NeuroTRACK).

OPR-003

Human spinal cord organoids to model C9orf72 ALS and test new therapies in vitro.

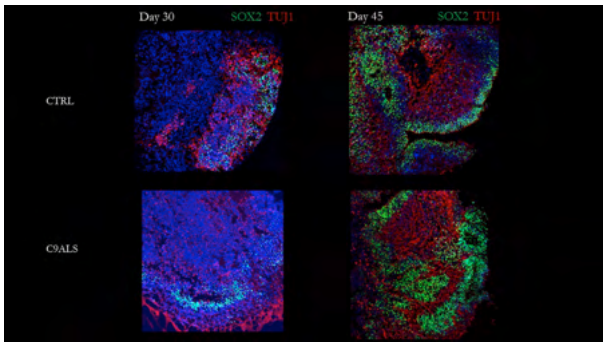
G. Costamagna [1], N. Galli [1], M. Rizzuti [2], B. Frizzi [2], F. Biella [2], M. Taiana [2], S. Ghezzi [2], G. Comi [1], I. Faravelli [1], M. Nizzardo [2], S. Corti [1]

[1] Department of Neurosciences, Milano, Italy, [2] University of Milan Dino Ferrari Center Department of Pathophysiology and Transplantation (DEPT) Neuroscience Section IRCCS Foundation Ca' Granda Ospedale Maggiore Policlinico Milan Italy, Milan, Italy

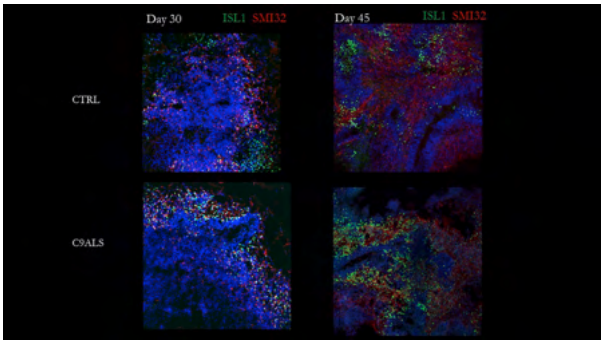
Background and aims: Amyotrophic lateral sclerosis (ALS) is an incurable neurodegenerative disease. Underlying genetic pathomechanisms include the C9orf72 repeat expansion, the most frequent genetic cause of ALS (C9ALS) in Europe and North America. Despite recent progress in unraveling C9ALS pathogenesis, reliable disease models and disease-modifying therapies still lack. Here, we aim to model C9ALS in vitro using 3D human spinal cord organoids (SCOs).

Methods: We differentiated C9ALS induced pluripotent stem cells (iPSCs) and isogenic controls using a free-floating 3D-culture method. We generated SCOs with a modified Lancaster's protocol promoting neural caudalization and ventralization. Then, we treated C9ALS SCOs with morpholino antisense oligonucleotides (MO) against C9Orf72 repeat expansion. Finally, we assessed the differentiation of organoids at different time points with immunohistochemical and qPCR analysis.

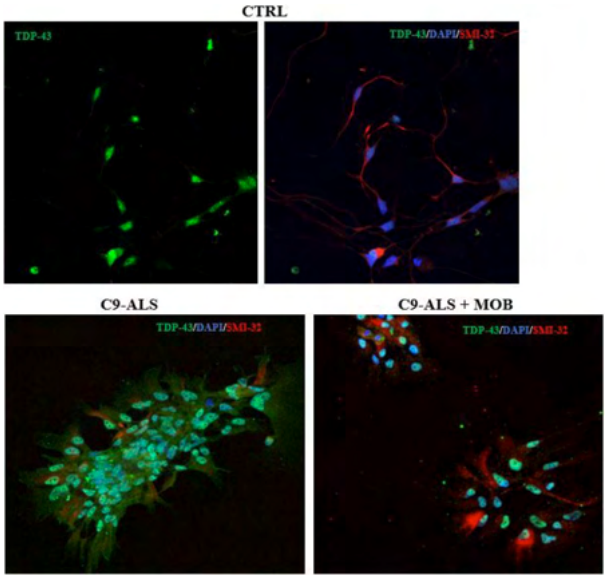
Results: We obtained isogenic and C9ALS SCOs displaying different co-existing neuronal subpopulations. SCOs expressed neural progenitor, pan-neuronal, astrocyte, motor neuron, and rostrocaudal markers, including markers of cervicobrachial spinal cells. Compared to controls, C9ALS organoids exhibited increased dipeptide repeat proteins (DPRs) levels, DNA damage markers associated with C9orf72 expansion, and cytoplasmic inclusions of translocated TDP-43, C9ALS-specific disease hallmarks. Gene expression analysis using qPCR reported differential expression of genes associated with DNA damage and motor neurons in MO treated C9ALS organoids.



Confocal microscopy imaging showing markers of neural precursors (SOX2) and early proliferating neurons (TUJ1) in C9ALS spinal cord organoids and isogenic controls at day 30 and day 45.



Confocal microscopy imaging showing motor neuron markers (Islet and Smi32) in C9ALS spinal cord organoids and isogenic controls at day 30 and day 45.



Confocal microscopy imaging displaying intracytoplasmic translocated TDP43 (green signal) in motor neurons from dissociated organoids possibly rescued by morpholino (MOB) treatment.

Conclusion: SCOs represent a valuable system for modeling features of C9ALS pathology, investigating C9ALS pathomechanisms, and testing possible new treatments in vitro.

Disclosure: The authors report no disclosures.

OPR-004

Nusinersen in adults with 5q spinal muscular atrophy: a systematic review and meta-analysis

M. Gavriilaki [1], M. Moschou [1], V. Papaliagkas [1], K. Notas [1], E. Chatzikyriakou [1], G. Zafeiridou [1], S. Papagiannopoulos [1], M. Arnaoutoglou [1], V. Kimiskidis [1]
[1] *Thessaloniki, Greece*

Background and aims: Nusinersen has been thoroughly studied in clinical trials of infants and children with 5q spinal muscular atrophy (SMA) and has gained approval for the treatment of all SMA types and patients of all ages. Data on nusinersen administration in adults are scarce, based on real-world evidence.

Methods: The purpose of this meta-analysis is to provide the first review of the literature regarding the efficacy and safety of nusinersen in patients older than 12 years of age with genetically confirmed 5q-SMA. We systematically searched MEDLINE, EMBASE, the Cochrane Library and grey literature through December 2020. Cross-sectional studies, case reports, review articles and/or studies with follow-up less than 6-months were excluded. Two reviewers screened eligible studies, extracted data, and assessed risk of bias (RoB).

Results: We included 11 records (seven case reports, four cohorts) enrolling 428 SMA patients older than 12 years with a follow–up of at least 6–months (Table 1). PRISMA flow diagram is presented at Figure 1. Clinically meaningful improvement (≥3-points) of Hammersmith Functional Motor Scale was observed in 35.3% (95%CI 22.1–49.7) and 43.7% (95%CI 35.7–51.6) of the patients during short–term (≤6-months) and long-term (>6-months) follow–up, respectively. Severe adverse events were reported in 3.3% (95%CI 0.4–6.2); treatment withdrawal rate was 2.8% (95%CI 1.2–4.4) (Table 2).

Figure 1. PRISMA Flow Diagram

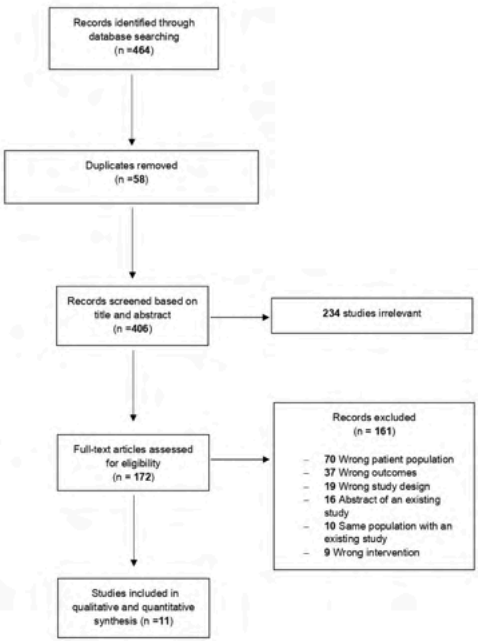


Figure 1. PRISMA Flow Diagram

First Author	Study Type	Number of Patients (N)	N SMA type 1	N SMA type 2	N SMA type 3	N SMA type 4	Age at treatment, years (range)	Ambulant (%)	Previous surgery for scoliosis and/or severe scoliosis (%)	RoB *
DeWel 2020	Cohort	48	0	15	30	3	37.1 (20–66)	20.8	41.7	Low risk
Faraveli 2019	Case series	12	0	0	12	0	28.5 (15.0-34.8)	83.3	0	Fair
Hagenacker 2020	Cohort	139	2	47	89	1	37 (16–65)	37	22	Low risk
Inan 2020	Case series	40	0	4	36	0	34.4 (19-60)	42.5	15	High risk
Jochmann 2020	Case series	7	0	4	3	0	45 (20-68)	14.2	42.8	Low risk
Maggi 2020	Cohort	116	0	13	103	0	34 (18–72)	34.5	13.8	Low risk
Moshe-Lilie 2020	Case series	22	0	9	13	0	36 (20-71)	9	77	Low risk
SHINE study 2020	Case series	7	0	1	6	0	14.4 (13-16)	71.4	na	Fair
Veerapandiyan 2020	Case series	12	1	4	7	0	22 (12–52)	25	66.7	Low risk
Walter 2019	Cohort	19	0	0	19	0	34 (18–59)	63	0	Low risk
Yeo 2020	Case series	6	0	0	6	0	29.9 (24.9-56.5)	67	0	Low risk
Total		428	3	97	324	4		36.4%	24%	

SMA: Spinal muscular atrophy, na: non-applicable
* Risk of Bias (RoB) was assessed using Newcastle-Ottawa scale for cohort studies and case series according to a tool proposed by Murad et al,BMJ Evidence-Based Medicine 2018

Table 1. Baseline characteristics and risk of bias assessment of the 11 studies.

First Author	Number of Patients that received Nusinersen	Length of nusinersen treatment, range (months)	Number of patients with severe adverse events	Severe adverse events description	Number of patients who stopped treatment	Reasons of treatment withdrawal
DeWel 2020	16	6 to 14	0	na	0	na
Faraveli 2019	12	6	0	na	0	na
Hagenacker 2020	139	6 to 14	0	na	4 (n=2)	Adverse drug reactions or procedure related events (n=2), patient's wish
Inan 2020	40	3 to 9	0	na	2	Difficulty of procedure (n=2)
Jochmann 2020	7	2 to 10	0	na	1	Sacral pressure ulcer close to the injection site (n=1)
Maggi 2020	116	6 to 14	6	Hospitalization for postprocedure headache (n=1), renal colic requiring hospitalisation (n=1)	2	Lack of subjective benefit and poor tolerability of repeated lumbar puncture (n=2)
Moshe-Lilie 2020	10	6 to 24	3	Bowel and bladder incontinence (n=1), bacterial meningitis (n=1), death by respiratory failure in the setting of pneumonia shortly after treatment initiation (n=1)	3	Lack of improvement (n=1), recurrent pneumonia (n=1), or proteinuria (n=1)
SHINE study 2020	7	64 to 82	3	Post-lumbar puncture headache that was considered severe and resolved with treatment (n=1), Pyuria and hematuria (n=1), Vesicoureteral reflux and pyelonephritis (n=1)	0	na
Veerapandiyan 2020	12	4 to 26	2	Hospitalization for an epidural blood patch (n=1), generalized tonic clonic seizure a day after the first maintenance dose (n=1)	0	na
Walter 2019	19	2 to 10	0	na	2	Subjective safety concerns regarding hydrocephalus development (n=1), planned pregnancy (n=1)
Yeo 2020	6	14 to 25	2	Hospitalization for a fall with comminuted sacral compression fractures (n=1) and for leg cellulitis in the setting of chronic lower extremity lymphedema (n=1)	0	0

na: non-applicable

Table 2. Data regarding safety, adverse events and treatment withdrawal as defined and reported in each study.

Conclusion: Despite the low quality of evidence and the unmet need for randomized data to establish the safety and efficacy of nusinersen in adults, our meta-analysis confirms that nusinersen is a valuable treatment option for patients with longer-disease duration. Registration: PROSPERO database CRD42020223109

Disclosure: Nothing to disclose..

Multiple Sclerosis: Biomarkers and genetics

OPR-005

Effect of BDNF Val66Met polymorphism on hippocampal subfields in multiple sclerosis patients

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Background and aims: Brain-derived neurotrophic factor (BDNF) Val66Met polymorphism was shown to affect BDNF function. We aimed to explore BDNF Val66Met polymorphism effect on hippocampal subfields and its role in cognitive functioning in MS patients.

Methods: Using 3T scanner, we obtained dual-echo and 3DT1-weighted sequences from 50 MS patients and 15 healthy controls (HC). MS patients also underwent genotype analysis of BDNF, neurological and neuropsychological evaluation. Hippocampal subfields were segmented by using Freesurfer.

Results: The BDNF Val66Met polymorphism was found in 22 MS patients. Compared to HC, MS patients had lower volume in: bilateral hippocampus-amygdala transition area (HATA); cornus ammonis (CA)1, granule cell layer of dentate gyrus (GCL-DG), CA4 and CA3 of left hippocampal head; molecular layer (ML) of left hippocampal body; presubiculum of right hippocampal body and right fimbria. Compared to BDNF Val66Val, Val66Met MS patients had higher volume in: bilateral hippocampal tail; CA1, ML, CA3, CA4 and GCL-DG of left hippocampal head; CA1, ML and CA3 of left hippocampal body; left HATA and presubiculum of right hippocampal head. In MS patients, lower volume in left hippocampal tail was associated with worse visuo-spatial memory performance; lower volume in left hippocampal head with worse performance in semantic fluency; lower volume in bilateral hippocampal tail with worse performance in executive functions; and lower volume in presubiculum of right hippocampal head with higher fatigue scores.

Conclusion: BNDF Val66Met polymorphism resulted as a protective factor in MS. BDNF genotype might be a potential biomarker for predicting cognitive prognosis, and an interesting target to study for neuroprotective strategies.

Disclosure: Nothing to disclose..

OPR-006

Genetic factors implicated in the response to fingolimod in MS patients: results from a pharmacogenetic meta-analysis

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Background and aims: Multiple Sclerosis (MS) is a complex disease with high heterogeneity in terms of clinical presentation and treatment response. Pharmacogenetics can help to develop a more personalized approach and to improve disease management. Here we report the results of a genome-wide association study (GWAS) on fingolimod (FTY)-treated relapsing-remitting MS patients.

Methods: We included four cohorts of FTY-treated MS patients from San Raffaele Hospital in Milan, Italy (OSR1: 246 patients, OSR2: 98 patients), Brigham and Women's Hospital in Boston, USA (USA: 136 patients) and the Centre Hospitalier Universitaire de Toulouse, France (CHUT: 81 patients). We classified treatment response according to the NEDA (no evidence of disease activity) criterion at two years and time to first relapse (TFR). We performed a GWAS separately on each cohort and meta-analyzed them using a fixed-effect model.

Results: Three genome-wide significant variants were associated with TFR: rs9397818A on chr6 increases the risk of an earlier relapse and has an eQTL effect in whole blood on TFB1M, key to mitochondrial gene expression, and TIAM2, implicated in endothelial function and cell migration; rs2071572A is a risk allele intronic to synaptotagminV, involved in exocytosis of secretory vesicles, with an eQTL effect in brain cortex; finally the risk allele rs6124768A maps to CD40 locus and increases its expression according to a public eQTL database. No significant variants were identified in the NEDA analysis.

Conclusion: Genetic variants possibly implicated in cell migration, neuronal functions and immune response were associated with response to FTY. Functional studies are ongoing to validate our results.

Disclosure: Laura Ferrè has nothing to disclose.

OPR-007

Brain dysconnectivity damage contributes to neurofilament light level increase in multiple sclerosis: Multicenter study

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Background and aims: The predictive value of conventional lesion characteristics for clinical course and biomarkers in multiple sclerosis (MS) has been limited. This clinico-radiological paradox may be partly resolved by connectivity-based approaches incorporating the distribution and extent of brain network aberrations due to T2-hyperintense lesions. Using individual brain dysconnectivity mapping based on tractography, we tested the longitudinal associations between putative brain network involvement and levels of serum neurofilament light chain (sNfL), which is a proposed biomarker for axonal damage.

Methods: MS patients (n=328, mean age 42.9 years, 71% female) were prospectively enrolled at four European MS centres, reassessed at two-year follow-up (n=280). 3T magnetic resonance imaging (MRI) data were processed at one site using a harmonized pipeline. Disconnectome maps were calculated using BCBtoolkit, based on the individual lesion maps. Global disconnectivity (GD) was defined as the average probability of disconnectome across all voxels in each patient's white matter. sNfL concentrations were measured by an ultrasensitive Single molecule array (Simoa) assay. Robust linear mixed models (rLMM) with GD as dependent variable, patient as random factor, and sNfL, age, sex, diagnosis and treatment as fixed factors were run.

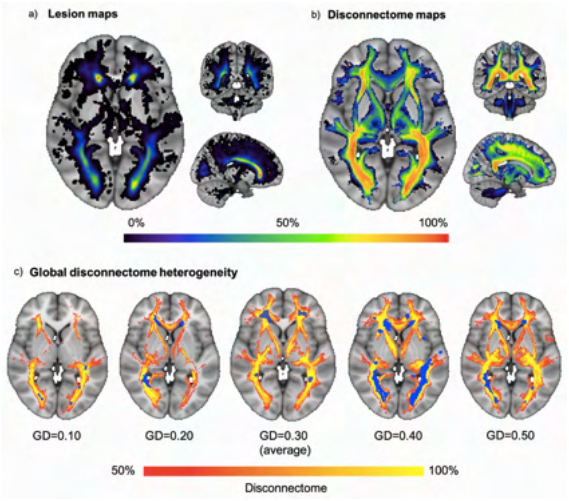

Figure 1. An overview with representative example slices of the probability distribution of A) lesion and B) disconnectome maps, along with examples of different levels of global dysconnectivity in C).

Results: rLMM revealed significant associations between GD and sNfL (t=2.30, p=0.022), age (t=5.01, p<0.001), and diagnosis (PMS; t=1.97, p<0.05), but no significant associations for sex, treatments or sNfL change.

	GD				t2lv			
Predictors	*Estimates*	*CI*	*t*	*p*	*Estimates*	*CI*	*t*	*p*
(Intercept)	-1.16	-1.77 – -0.55	-3.70	**<0.001**	-0.70	-0.83 – -0.56	-10.29	**<0.001**
sNfL	0.14	0.08 – 0.21	4.62	**<0.001**	0.05	0.02 – 0.09	2.89	**0.004**
Age	0.24	0.12 – 0.36	3.90	**<0.001**	0.08	-0.01 – 0.17	1.68	0.094
Sex [Female]	0.13	-0.08 – 0.34	1.19	0.234	0.03	-0.08 – 0.14	0.54	0.592
diagnosis [PMS]	1.39	0.70 – 2.09	3.94	**<0.001**	0.37	-0.00 – 0.74	1.95	0.052
diagnosis [RRMS]	0.52	-0.11 – 1.15	1.63	0.104	0.11	-0.03 – 0.26	1.56	0.121
treatment [Effective]	0.44	0.18 – 0.70	3.29	**0.001**	0.17	0.05 – 0.29	2.71	**0.007**
treatment [Highly-effective]	0.73	0.43 – 1.04	4.75	**<0.001**	0.35	0.15 – 0.55	3.49	**0.001**
Observations	294				294			
R^2 / R^2 adjusted	0.261 / 0.243				0.160 / 0.139			

Table 1. Linear regression for sNfL at baseline with global disconnectome maps and T2-lesion volume.

	GD				t2lv			
Predictors	*Estimates*	*CI*	*t*	*p*	*Estimates*	*CI*	*t*	*p*
(Intercept)	-1.11	-2.16 – -0.07	-2.09	**0.037**	-0.66	-1.31 – -0.01	-1.98	**0.047**
sNfL	0.03	0.00 – 0.05	2.30	**0.022**	-0.00	-0.02 – 0.01	-0.74	0.461
Timepoint	-0.00	-0.01 – 0.01	-0.79	0.432	0.02	0.01 – 0.02	7.41	**<0.001**
Age	0.32	0.19 – 0.44	5.01	**<0.001**	0.22	0.15 – 0.30	5.68	**<0.001**
Sex [Female]	0.11	-0.16 – 0.37	0.78	0.434	0.09	-0.08 – 0.25	1.01	0.312
diagnosis [PMS]	1.06	0.01 – 2.11	1.97	**0.049**	0.38	-0.27 – 1.04	1.15	0.249
diagnosis [RRMS]	1.01	-0.04 – 2.06	1.89	0.059	0.40	-0.25 – 1.05	1.20	0.229
treatment [Effective]	0.01	-0.02 – 0.04	0.85	0.394	-0.01	-0.03 – 0.01	-1.31	0.192
treatment [Highly-effective]	0.01	-0.02 – 0.04	0.86	0.389	0.00	-0.01 – 0.02	0.46	0.644
sNfL * Timepoint	-0.01	-0.03 – 0.00	-1.65	0.098	0.01	-0.00 – 0.01	1.87	0.061
Random Effects								
σ^2	0.00				0.00			
τ_{00}	1.06 ID				0.41 ID			
ICC	1.00				1.00			
N	296 ID				296 ID			
Observations	506				506			
Marginal R^2 / Conditional R^2	0.109 / 0.998				0.116 / 0.999			

Table 2. Robust linear mixed models predicting sNfL with global disconnectome maps and T2-lesion volume.

Conclusion: In our longitudinal prospective MS cohort, we showed significant associations between GD and sNfL. Our results demonstrate that the extent of global brain dysconnectivity is sensitive to a systemic biomarker of axonal damage in MS.

Disclosure: This work was supported by the European Commission, Instituto de Salud Carlos III, Spain, the Italian Ministry of Health, the German Ministry of Science, the Norwegian Research Council and Biogen Norway.

OPR-008

Multilayer network analysis relates molecular and clinical features of multiple sclerosis

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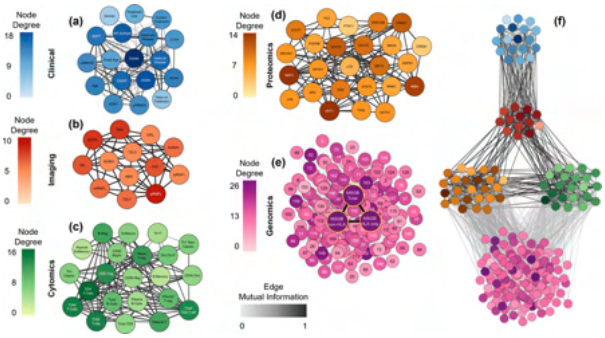
Background and aims: Multiple Sclerosis is a complex disease covering a wide range of biological scales, from genes, to proteins and cells, to tissue damage (assessed by imaging) and finally to the phenotype. However, the exact interactions among each scale remain unclear. As a result, current methods for diagnosis and prognosis are often imprecise because they fail to capture this multi-scale level of complexity in MS.

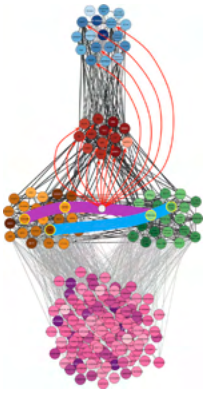
Methods: Here, we conducted a systems biology study based on multi-level networks and regression models, which allows us to analyse multi-omics, imaging and clinical data obtained from MS patients to both aid in diagnosis, prognosis and increase our understanding of the underlying pathogenesis. Multi-scale networks were constructed using genomics, proteomics, cytomics, imaging (MRI and OCT), and clinical data from a prospective cohort of 350 MS patients and 90 matched controls from four MS centers and with two years follow-up. Structural networks were constructed using mutual information and boolean simulations, and then run on the proteomics and cytomics networks to identify pathways associated with MS and phenotype (mild vs severe cases).

Illustration of network construction. The data from each layer is taken from the cohorts and used to create networks, where the nodes are the elements in the dataset (SNPs, proteins, cell types, OCT/MRI, and phenotypic data).



Topology of individual layer networks and the combined 5-layer network, constructed using all MS patients' data.

Results: We identified several regression models predicting phenotype based on protein-cell pathways, which outperformed genome–phenotype correlations. The most prominent pathway was GSK3AB – B memory cell pathway, that significantly predicted the phenotype (disability and brain atrophy), followed by IKBA – effector B cells and HSBP1-memory B cells.



Example of one pathway (identified from the Boolean simulations) that significantly predicts various MS phenotypes.

Conclusion: The pathways identified in this analysis may be pursued as therapeutic targets or biomarkers for developing new therapeutics for MS.

Disclosure: This work was supported by the European Commission, Instituto de Salud Carlos III, Spain, the Italian Ministry of Health, the German Ministry of Science, the Norwegian Research Council and Biogen Norway.

OPR-009

Multiple sclerosis associated HLA variants affect the immunological T lymphocytes repertoire

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Background and aims: Genetic predisposition to multiple sclerosis (MS) includes >200 genetic loci, with the major histocompatibility complex (MHC) region accounting for 32 independent associations. We aim to investigate the impact of MHC MS-risk alleles on T lymphocytes repertoire in MS.

Methods: 183 untreated relapsing-remitting MS subjects have been studied. Class I and II HLA alleles were inferred from whole-genome genotyping data using SNP2HLA and Beagle_v3.3 tools. T-cell receptors (TCR) CD3 sequences were obtained from whole blood DNA according to the ImmunoSEQ hsTCRB kit (Adaptive Biotechnologies®). The weighted HLA-risk score (wHRS) was calculated for each individual. The inverse of the Simpson's Index (INV.S) was calculated as representative of immune repertoire diversity. Statistical analyses were performed within R environment and plink v.1.9.

Results: After quality controls and downsampling, the final set was composed by 144 individuals and 30
MS-risk MHC loci. Four loci showed association with INV.S (beta referring to the MS-risk allele): HLA DRB1 15*01 (p=0.014, beta=-1.02), rs11751659 (p=0.02, beta=0.79), rs9271366 (p=0.003, beta=-1.14),
SNP_DRB1_32660116_A (p=0.036, beta=-0.5). A mild association was found between INV.S and wHRS (p=0.049), with individuals with a higher wHRS showing a lower diversity. Additionally, individuals carrying the risk allele showed a different percentage of clonotypes occupying the 10% of the repertoire, suggesting an expansion of certain clonotypes in the presence of the risk allele.

Conclusion: MS-risk MHC loci appear to influence TCR repertoire in MS patients, with the risk alleles reducing the diversity and inducing an expansion of specific clonotypes. Detailed analyses are ongoing to better define the amplified clonotypes and their role.

Disclosure: Authors declares no competing interests regarding this study.

OPR-010

Cerebrospinal fluid levels of CXCL12 and Osteopontin: potential early marker of primary progressive multiple sclerosis

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Background and aims: Both degenerative and inflammatory processes characterize primary progressive multiple sclerosis (PPMS). Like relapsing-remitting MS (RRMS) and secondary progressive MS, inflammatory infiltrates build up in the meningeal space, resulting in a severe disease course. PPMS patients represent an interesting cohort to investigate in vivo processes and possible biomarkers underlying disease progression.

Methods: Levels of 34 pro and anti-inflammatory cytokines and chemokines in the cerebrospinal fluid (CSF) were evaluated at the diagnosis in 16 PPMS and 80 RRMS patients. All patients underwent clinical evaluation, including Expanded Disability Status Scale (EDSS) assessment and a 3-T brain MRI with detection of white matter and cortical lesion number and volume and global and regional cortical thickness.

Results: Higher levels of CXCL12 (OR=3.97, CI95%[1.34–11.7]) and the monocyte–related osteopontin (OR=2.24, CI95%[1.01–4.99]) were associated with the diagnosis of PPMS, while levels of IL10 (OR=0.28, CI95%[0.09–0.96]) were significantly increased in RRMS group. No associations were found between examined molecules and EDSS; CXCL12 levels correlated with both increased GM lesion number and volume (p=0.001, r=0.832 and r=0.821, respectively). The pathway analysis confirmed the chronic inflammation is occurring in PPMS.

Conclusion: At the time of diagnosis, a specific CSF protein profile can recognize the presence of early intrathecal inflammatory processes, possibly stratifying PPMS with respect to RRMS. Elevated CSF levels of CXCL12 and Osteopontin suggested a key role of brain innate immunity and glia activity in MS. Therefore, these molecules could represent useful candidate biomarkers of MS progression and could have important implications for the pathogenesis and treatment of progressive MS.

Disclosure: No

Neurogenetics 1

OPR-011

Efficacy and safety results of the avalglucosidase alfa phase 3 COMET trial in late-onset Pompe disease patients

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Background and aims: The Phase 3 COMET trial (NCT02782741/Sanofi Genzyme) compares avalglucosidase alfa (n=51), a recombinant human GAA enzyme replacement therapy specifically designed for enhanced M6P-receptor targeting and enzyme uptake aimed at increased glycogen clearance, and alglucosidase alfa (n=49) in treatment-naïve patients with late-onset Pompe disease.
Methods: The primary objective was to determine the effect of avalglucosidase alfa on respiratory muscle function. Secondary/other objectives include effects on functional endurance, inspiratory/expiratory muscle strength, lower/upper extremity muscle strength, motor function, and health-related quality of life, and safety.
Results: At Week 49, change (LS mean±SE) from baseline in upright forced vital capacity (FVC) %predicted was 2.43% greater with avalglucosidase alfa (2.89% ±0.88%) than with alglucosidase alfa (0.46% ±0.93%). The primary study objective, achieving statistical non-inferiority (p=0.0074), was met. Testing for superiority was borderline significant (p=0.0626). Avalglucosidase alfa treatment resulted in a 30.01-meter and 4.71% greater improvement in the 6-Minute Walk Test (32.21±9.93 vs. 2.19±10.40 meters; 5.02±1.54 vs. 0.31±1.62%predicted). Positive results for avalglucosidase alfa were seen for all secondary and other efficacy endpoints. Treatment-emergent adverse events (AEs) occurred in 86.3% of avalglucosidase alfa-treated and 91.8% of alglucosidase alfa-treated participants. Five participants withdrew, four due to AEs, all with alglucosidase alfa. Serious AEs occurred in eight avalglucosidase alfa-treated and 12 alglucosidase alfa-treated participants. IgG antidrug antibody responses were similar for both. High titers (12,800) and neutralizing antibodies were more common for alglucosidase alfa.
Conclusion: Results demonstrate improvements in clinically meaningful outcomes and a more favorable safety profile with avalglucosidase alfa versus alglucosidase alfa.
Disclosure: The COMET trial is sponsored by Sanofi Genzyme.

OPR-012

Plasma neurofilaments as biomarkers in frontotemporal dementia associated with C9orf72 and GRN mutations

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Background and aims: C9orf72 and progranulin (GRN) mutations are the main genetic causes of frontotemporal dementia (FTD) and, for C9orf72, amyotrophic lateral sclerosis (ALS). Upcoming targeted therapies highlight the importance of easily-accessible, reliable biomarkers for the preclinical and clinical follow-up. We aimed to evaluate longitudinal changes of plasma neurofilament light chain (NfL) in mutation carriers and in healthy controls (HC).
Methods: Our study cohort consists of 352 individuals including 102 FTD and/or ALS patients (54 C9orf72 carriers and 48 GRN carriers), 85 presymptomatic carriers (PS: 48 C9orf72 and 37 GRN), and 165 HC. Participants were recruited through PREV-DEMALS and Predict-PGRN protocols, and the national research network on FTD/ALS. They underwent up to six blood samplings during a mean follow-up of four years. NfL dosage was performed with the SIMOA technique.
Results: In HC, NfL increased with age at sampling (r=0.766, p<0.0001) and slightly progressed over time, with a mean change rate of 4%/year. Patients had higher NfL compared to HC and PS (Fig.1). The causal gene had a major effect, GRN carriers having higher baseline values (p=0.014) and greater progression compared to C9orf72 carriers (p=0.016) (Fig.2). We proposed thresholds to differentiate symptomatic carriers from HC at each age class. NfL in PS were comparable to HC at baseline, with a subset displaying increased progression.

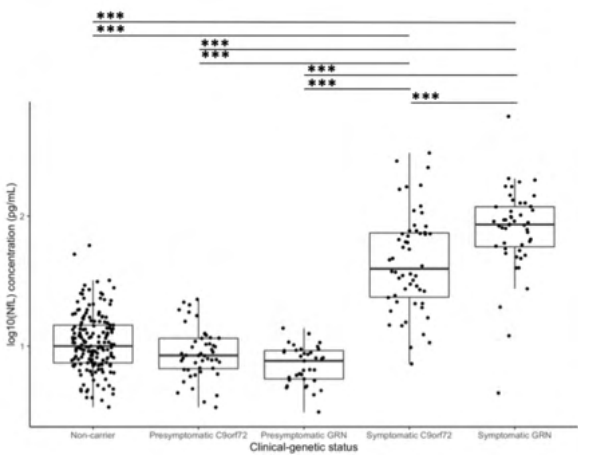

Figure 1. Baseline plasma NfL levels in patients, presymptomatic carriers and controls. Comparisons were performed with general linear model to account for all variables (gene/status, age, sex) and post hoc test (*: p<0.05; **: p<0.01; ***: p<0.001).

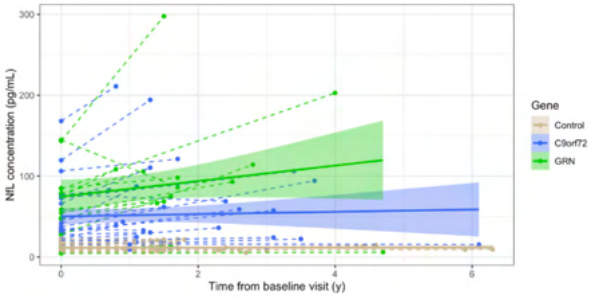

Figure 2. Longitudinal changes in mutation carriers and healthy controls. NfL variations from the first to the last observation, for 44 patients and 36 controls with longitudinal sampling, at the individual and group level (linear mixed-effects model).

Conclusion: NfL levels prove their usefulness in tracking the degenerative process in C9orf72 and GRN mutations. Combined with other biomarkers, they will hopefully allow to identify PS close to their clinical conversion, and define the optimal time window to deliver targeted therapies.
Disclosure: The authors declare no disclosures relevant to the abstract. ILB served as a member of advisory board for Prevail Therapeutics, and of steering committee for Alector, outside of the present work.

OPR-013

Gene association networks and miRNA-gene interactions reveal pathological pathways involving IL6 in Parkinson's disease

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Background and aims: Parkinson´s Disease (PD) is a complex disorder characterized by multiple contributing factors. The study investigated SNPs regulating interactions among genes, miRNA and their targets in order to highlight novel biomarkers or therapeutic targets for the treatment and management of PD.
Methods: The study included 342 patients affected by sporadic PD and 503 control samples. The OpenArray technology was utilized to screen patients for 120 SNPs selected by literature and bioinformatic approach, giving preference to non-coding variants that may affect regulatory gene networks relevant to PD. Statistical and bioinformatic analysis were performed to assess the association with PD and identify network of genes and miRNAs interactions.
Results: 26 SNPs were associated with PD risk, of which 12 SNPs were significant eQTL variants in different brain regions involved in motor and non-motor symptoms. Moreover, 11 novel susceptibility genes for PD were identified, which may alter multiple signaling pathways critically involved in cellular homeostasis and dopaminergic neurons wiring. A network of interconnected genes (APOE, CLU, IL6, IL7R, IL12B, INPP5D, MAPK1, MEF2C, MIF, TNFSF14) highlighted a major regulatory role of IL6 in the network. The study of miRNA-target gene networks highlighted a possible role of miR-499a and miR-196a2 in multiple neuro-inflammatory and neurodegenerative mechanisms in PD.
Conclusion: The study highlighted different networks of genes and miRNA-target gene interactions in PD. In particular, IL6 stands out as the most promising candidate either as prognostic biomarker of disease or as therapeutic target to fight neuro-inflammation and neurodegeneration in PD patients.
Disclosure: Nothing to disclose.

OPR-014

Phenotypic features and disease progression of the m.8344A>G MT-TK gene variant: MERRF syndrome and beyond

Y. Shiau Ng [1], A. Lim [1], F. Gruosso [2], A. Blain [1], R. Thomas [1], A. Schaefer [1], M. Mancuso [3], R. Taylor [1], D. Turnbull [1], R. McFarland [1], G. Gorman [1]
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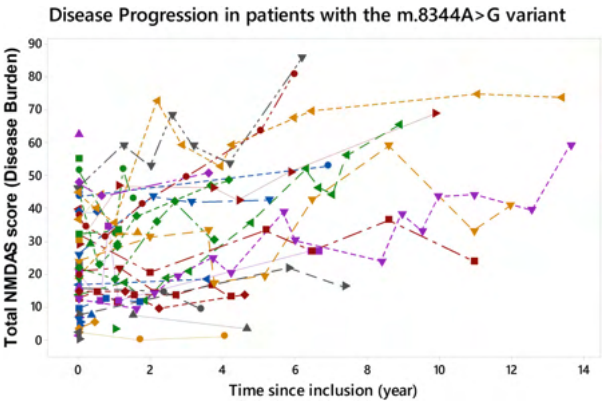
Background and aims: Myoclonic epilepsy with ragged red fibres (MERRF) is a classic syndrome of mitochondrial DNA disease most commonly associated with the pathogenic m.8344A>G MT-TK gene variant. While phenotypic heterogeneity has been extensively described, disease progression is poorly characterised.
Methods: Single national centre, observational study (2009–2020). Data derived from the UK Mitochondrial Disease Patient Cohort.
Results: We identified 64 individuals (42 women) from 30 pedigrees and mean (SD; range) age of last follow up was 46.9 (17.4; 3–73) years. Common neurological features were proximal myopathy (73%), cerebellar ataxia (62%), seizures (59%), myoclonus (57%) and swallowing problems (49%). Other systemic manifestations comprised gastrointestinal dysmotility (51%), lipomatosis (36%), cardiac (29%) and respiratory involvement (29%). Sixteen individuals were asymptomatic. Myoclonus was associated with both epilepsy (2=19.5, p<0.001) and cerebellar ataxia (2=11.2, p=0.001). Mean (SD) m.8344A>G blood heteroplasmy was significantly higher in clinically affected individuals than asymptomatic carriers [71% (18%) vs 48% (17%), p<0.001]. We measured total disease burden using Newcastle Mitochondrial Disease Adult Scale and demonstrated the rate of disease progression was variable between patients (Figure 1); m.8344A>G blood heteroplasmy was a weak predictor of disease burden based on a multivariate regression model (p=0.015, R^2= 0.485).



Disease Progression in adult patients with the m.8344A>G variant

Conclusion: Our findings provide insight into the natural history of m.8344A>G-related mitochondrial disease. The variability of phenotypic expression and disease progression has significant implications on the design of future clinical trials with robust modelling of disease progression necessitating wider datasets through international collaboration.
Disclosure: Nothing to disclose.

OPR-015

Efficacy and Safety With >3 Years of Inotersen Treatment for the Polyneuropathy of Hereditary Transthyretin Amyloidosis

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Background and aims: Hereditary transthyretin amyloidosis is a progressive, debilitating, and ultimately fatal disease that causes multisystem dysfunction. Here we report long-term efficacy and safety for inotersen, an antisense oligonucleotide inhibitor of transthyretin protein production.

Methods: Patients completing the NEURO-TTR trial (NCT01737398) enrolled in its open-label extension (OLE; NCT02175004). Assessments included modified Neuropathy Impairment Score +7 (mNIS+7), Norfolk Quality of Life–Diabetic Neuropathy questionnaire (Norfolk QOL-DN), and safety monitoring. As of July 28, 2020, efficacy is reported for patients from Europe and North America and safety is reported for all patients.

Results: Patients who switched from placebo to inotersen in the OLE (n=39) demonstrated slowing of neurologic disease progression compared with natural history (based on placebo projection); mean mNIS+7 and Norfolk QOL-DN scores at OLE baseline/1/2/3 years were 102.7/111.2/113.6/112.3 and 61.2/59.0/63.5/67.7, respectively. Patients receiving inotersen for 51 months (15 months in NEURO-TTR + 36 months in OLE; n=67) continued to show benefit, with mean mNIS+7 and Norfolk QOL-DN scores at OLE baseline/1/2/3 years of 84.3/90.7/98.1/95.1 and 50.3/52.4/53.1/57.2, respectively. Few patients (6/135; 4.4%) had serious treatment-related adverse events; there were no treatment-related deaths. Under enhanced monitoring, there have been no reports of grade four thrombocytopenia or acute glomerulonephritis despite increased duration of exposure. No new safety concerns were identified.

Conclusion: Extended treatment with inotersen for over three years slowed progression of the polyneuropathy associated with hereditary ATTR, with greater benefit observed in patients who initiated inotersen earlier. Long-term results further highlight the importance of early treatment. Enhanced monitoring has reduced risks of severe thrombocytopenia and acute glomerulonephritis.

Disclosure: Funding was provided by Akcea Therapeutics, an Ionis Company, and editorial assistance was provided by ApotheCom.

OPR-016

Three Newly Recognized Likely Pathogenic Variants of the TTR Gene Causing Hereditary Transthyretin Amyloidosis

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Background and aims: Hereditary transthyretin amyloidosis (hATTR/ATTRv) is a progressively debilitating, clinically heterogeneous, fatal disease that results from deposition of insoluble amyloid fibrils in various organs and tissues. Symptomatic patients exhibit cardiomyopathy, polyneuropathy, or both, depending on the TTR variant. Early diagnosis of hATTR can be facilitated with genetic testing; however, such testing identifies variants of uncertain significance (VUS) in a minority of cases. Although most VUS reflect benign genetic variation present in the human genome, a small percentage of VUS have the potential to be pathogenic. The Akcea/Ambry VUS Initiative is dedicated to gathering molecular, clinical, and inheritance data for each TTR VUS identified via genetic testing programs to reclassify TTR variants to a clinically actionable status (eg, variant likely pathogenic [VLP]) where appropriate.

Methods: The classification criteria used here are based on recommendations from the American College of Medical Genetics. They are stringent and comprehensive, requiring multiple distinct lines of evidence supporting pathogenesis. Variants were assessed for reclassification based on the totality of evidence available.

Results: Three TTR variants have been reclassified from VUS to VLP, including p.A65V (c.194C>T), p.D58H (c.172G>C), and p.T80I (c.239C>T). In each case, the totality of genetic and clinical evidence provided strong support for pathogenicity. The new classification of each variant will be submitted to the NIH ClinVar database.

Conclusion: Based on multiple lines of evidence, three TTR VUS were reclassified as VLP, thus resulting in a high likelihood of disease diagnosis for those and all subsequent patients. Confirmed hATTR diagnosis can facilitate access to approved therapies.

Disclosure: Funding was provided by Akcea Therapeutics, an Ionis Company; editorial assistance was provided by ApotheCom and scientific support was provided by Ambry Genetics.

Neuroimaging

OPR-017

Disease severity in Progressive Supranuclear Palsy determines the relationship between tau burden and synaptic density

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Background and aims: The in-vivo relationship between synaptic loss and tau accumulation in Progressive Supranuclear Palsy (PSP) is key to understanding the impact of tauopathy on functional decline.

Methods: We determine the correlation between synaptic density and tau accumulation in PSP – Richardson's Syndrome using [11C]UCB-J and [18F]AV-1451 PET imaging, respectively. PSP patients (n=22, m:f 10:12, mean age ±sd: 70.8 ±8.6) were compared to age-/sex-/education-matched controls (n=17, m:f 9:8, mean age ±sd:68.8 ±7.0). Disease severity was assessed with the PSP rating scale.

Results: Across all brain regions, averaging across patients, there was a positive correlation between [11C]UCB-J and [18F]AV1451 binding. The direction of this correlation varied as a function of disease severity (beta=-0.03, t=-3.0, r=-0.58, p<0.01) (Fig 1). Between brain regions, comparing [18F]AV-1451 in a cortical region versus [11C]UCB-J in an anatomically connected sub-cortical area, revealed significant negative correlations (r≤0.4, p<0.05).

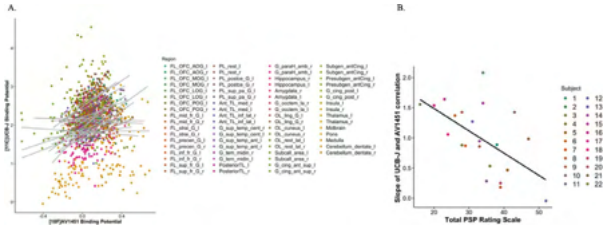

Figure 1. A) positive correlation between [11C]UCB-J and [18F] AV1451 non-displaceable binding potentials across all brain regions, B) Inter-individual variability in the correlations in A is determined by disease severity (PSP rating scale).

Conclusion: Brain regions with higher synaptic density are associated with a higher tau burden in PSP, while this association is a function of disease severity. Higher tau burden in cortical regions correlates with lower synaptic density in subcortical regions to which the cortical areas project. The effect of disease severity suggests a biphasic relationship between synaptic density and tauopathy: with densely connected regions initially more prone to tauopathy, followed by a loss of their connectivity in response to tauopathy. Given the importance of synaptic density for cognition, our study elucidates the pathophysiology of PSP and informs clinical trials' design at different disease stages.

Disclosure: Authors do not have any disclosures to make.

OPR-018

Increased Normal Appearing White Matter perfusion: an inflammatory marker in relapsing-remitting multiple sclerosis?

C. Lapucci [1], A. Stefanile [2], S. Zannino [2], M. Filippi [2], A. Cortese [2], C. Piantadosi [2], M. Salvetti [2], M. Inglese [1], T. Koudriavtseva [2]
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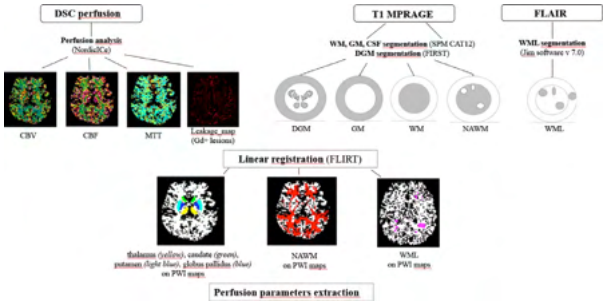
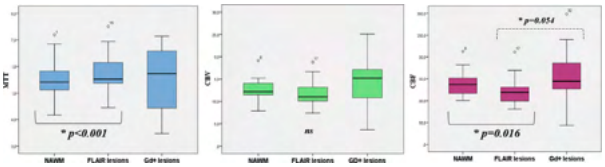
Background and aims: Brain hemodynamic changes by Dynamic Susceptibility Contrast enhanced perfusion (DSC) in Multiple Sclerosis (MS) have been evaluated in few studies. The aim is to compare relapsing and remitting (RR) MS patients by assessing Cerebral Blood Flow (CBF), Cerebral Blood Volume (CBV), Mean Transit Time (MTT) with DSC.

Methods: We included RRMS patients with (REL) and those without (REM) relapse in the previous two months. Clinical features were correlated with radiological findings (Pearson's test). ANOVA for repeated measures was used to compare perfusion between FLAIR, T1 GD lesions and Normal Appearing White Matter (NAWM).



MRI DSC analysis pipeline and co-registrations with structural images

Results: 45 RRMS patients [(22 REL/23 REM); mean (SD) age 41.3(8.4); female 77.8%; mean disease duration (DD) 12.8(7.1); mean ARR-1year and 2years 0.7(1.2) and 0.4(0.7); mean cumulative number of relapses (CNR) 3.9(3.6). CNR, ARR-1y and 2y were different between REL and REM ($p<0.001$). FLAIR and T1 lesion load correlated with DD ($p<0.001$, $r=0.8$), CNR ($p<0.05$, $r=0.6$) and z-MSFC ($p<0.05$, $r=-0.7$). In REM, correlations between NAWM CBV and DD ($p<0.05$, $r=-0.6$) or between NAWM CBF and both DD ($p=0.001$, $r=-0.7$) and ARR-1y ($p<0.05$, $r=0.4$) were found. MTT was lower whereas CBF was higher in NAWM than in FLAIR lesions ($p<0.05$). A trend indicating a higher perfusion of GD compared to FLAIR lesions was observed in CBF ($p=0.054$).



Comparisons of perfusion parameters among NAWM, FLAIR and GD lesions

Conclusion: In RRMS, a hyperperfusion of NAWM compared to FLAIR lesions was noted. Correlations between NAWM perfusion, DD and ARR-1y in REM patients seemed to suggest that an increased NAWM perfusion may be a radiological marker of inflammatory activity.

Disclosure: Authors have nothing to disclose

OPR-019

Progression of tau pathology across in-vivo stages of regional amyloid deposition

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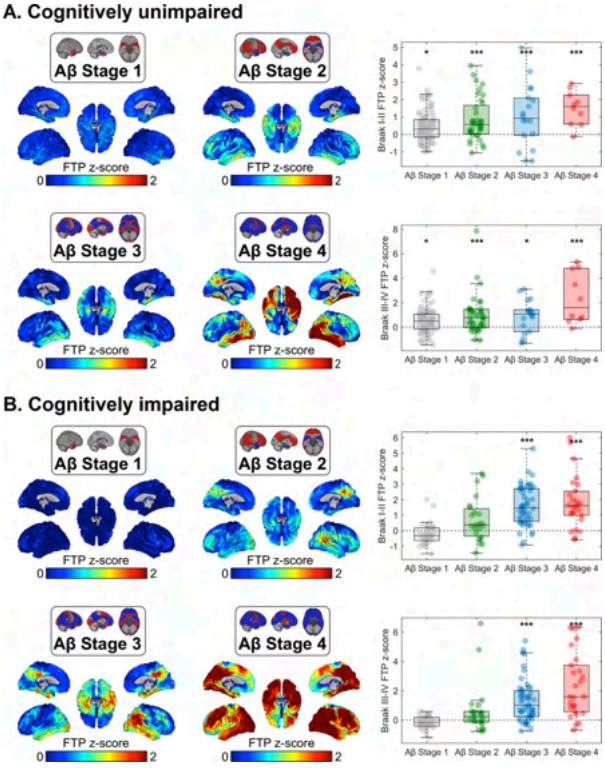
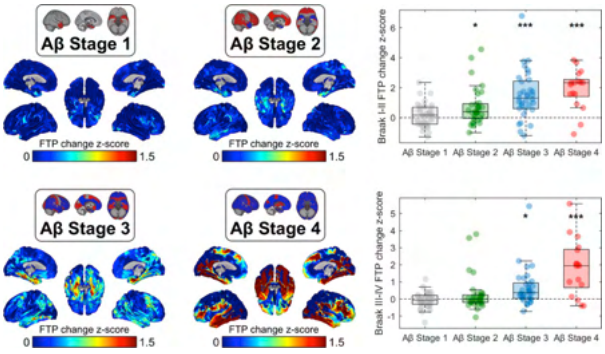
Background and aims: Previous research has consistently found widespread tau aggregation in the presence of global amyloid- (A) pathology, but the association of A pathology severity with tau accumulation remains unclear. Here, we studied tau aggregation in relation to progressive stages of regional A deposition as determined by a recently established A PET staging approach.
Methods: We examined 244 cognitively unimpaired (CU) and 180 impaired (CI) subjects with concurrent T1 MRI, 18F-Florbetapir-PET, and 18F-Flortaucipir-PET (FTP) scans. An A PET staging method was used to stratify participants into four progressive stages of A deposition. Linear regressions adjusted for age, sex, and, if appropriate, clinical diagnosis were used to assess regional FTP uptake across A stages in CU and CI individuals. Longitudinal tau accumulation in the whole sample was assessed with linear mixed effects models adjusted for the same covariates.
Results: A deposition followed a consistent regional hierarchy that allowed staging 99% of individuals. Cross-sectionally, gradual FTP uptake increases in Braak I-II were observed from stages 1 to 4 in CU, though only A stage four in CU and stages 3 and 4 in CI revealed widespread tau deposition compared to stage 0 (Fig. 1). Similarly, stage 2 was associated with longitudinal Braak I-II FTP increases, but only A stages 3 and 4 showed faster tau accumulation rates in regions exceeding Braak I-II (Fig. 2).



Cross-sectional flortaucipir PET patterns and flortaucipir uptake in Braak areas I-II and III-IV, referenced to Stage 0 subjects, across in vivo stages of regional amyloid deposition for cognitively unimpaired (A) and impaired (B) participants.



Longitudinal flortaucipir uptake change patterns and uptake change in Braak areas I-II and III-IV, referenced to Stage 0 subjects, across in vivo stages of regional amyloid deposition

Conclusion: The induction of severe and widespread tau pathology seems to occur at advanced stages of A deposition, which only cover a subpopulation of A-positive individuals as conventionally defined.
Disclosure: No disclosures

OPR-020

Differential diagnosis between common neurodegenerative dementias using metabolic brain images and machine learning

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Background and aims: FDG-PET scanning can reveal characteristic patterns of glucose hypometabolism in neurodegenerative dementias. Scans are usually assessed visually, however use of statistical analysis and machine learning provides additional information and increases FDG-PET clinical utility.
Methods: We analysed 67 FDG-PET scans from three dementia cohorts (27 Alzheimer's dementia (AD), eight dementia with Lewy bodies (DLB), 20 frontotemporal dementia (FTD)) and 12 normal controls (NC). Patients were diagnosed clinically and by visual assessment of FDG-PET scans. Scans were then pre-processed and "SingleCase" SPM t-maps created with SPM12. T-maps were classified into one of four (dementia syndrome or NC) categories by an expert reader. T-maps were imported to Orange and embedded with Inception v3 embedder (Google's deep neural network for image recognition). Embedded images were projected into two dimensional space using t-SNE. Five different machine learning methods (k-nearest neighbour (k-NN), logistic regression, neural network, SVM and random forest) were implemented and evaluated after 10-fold cross-validation. Their performance against clinical assessment and visual read was assessed.
Results: T-SNE visualization revealed a clear separation of patients from NC. There was some overlap between FTD and AD cohorts. DLB scans were clustered together, but placed within the AD cluster, Figure 1. Models achieved 75–82% classification accuracy. DLB was the most difficult class to predict. Confusion matrix of the best model (k-NN) is shown on Figure 2.

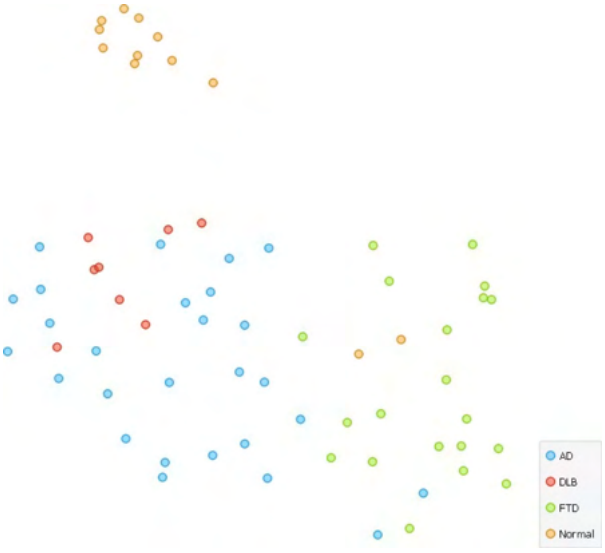

Image map after projection of images to two-dimensional space with t-SNE.

Predicted

Actual	AD	DLB	FTD	Normal	Σ
AD	22	4	1	0	27
DLB	1	7	0	0	8
FTD	3	0	16	1	20
Normal	0	0	2	10	12
Σ	26	11	19	11	67

Confusion matrix of k-NN model (82% overall accuracy).

Conclusion: Computer vision is gaining popularity. We presented its possible application to FDG-PET scans and "SingleCase" SPM t-maps in differential diagnosis of common dementias. Popular machine learning methods achieved high overall classification/diagnostic accuracy.
Disclosure: No disclosures.

OPR-021

Semiquantitative evaluation of brain glucose metabolism in anti-leucine-rich glioma- inactivated-1protein encephalitis

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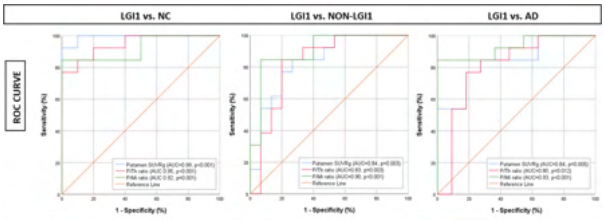
Background and aims: Putaminal hypermetabolism on [18F]fluorodeoxyglucose (FDG)-positron emission tomography (PET) in anti-leucine-rich, glioma-inactivated-1 protein (LGI1) antibody-associated autoimmune encephalitis (AE) has been previously reported. However, the accuracy of FDG-PET in distinguishing LGI1-AE from other AE's and neurodegenerative conditions is not known. Further, the presence of other subcortical and cortical metabolic abnormalities and prognostic value of FDG-PET in LGI1-AE is not clear.

Methods: Brain FDG-PET scans from 49 age- and sex-matched subjects (13 LGI1-AE, 15 non-LGI1-AE, 11 Alzheimer's disease (AD), 10 negative controls (NC)) were analyzed. Regions of interest were delineated using Automated Anatomic Labelling atlas. Putaminal standardized uptake value ratios (SUVR) with normalization to global brain (P-SUVRg), thalamus (P/Th) and midbrain (P/Mi) were evaluated for diagnostic accuracy. SUVRg was applied for all other analyses.

Results: P-SUVRg, P/Th and P/Mi were higher in LGI1-AE vs. non-LGI1-AE, AD and NC (all p<0.05, Bonferroni-corrected). P/Mi and P-SUVRg robustly differentiated LGI1-AE from NC, non-LGI1-AE and AD (areas under curve range 0.84-0.99; Fig. 1). Mediotemporal SUVRg was increased in both LGI1-AE and non-LGI1-AE vs. NC (p<0.05 for both). Additionally, LGI1-AE-patients showed hypometabolism in inferior frontal and parietal lobes, and hypermetabolism in globus pallidus, caudate, pons, olfactory and inferior occipital lobes when compared to NC (Fig. 2). Bilateral orbitofrontal and cingulate gyrus hypometabolism were associated with poorer outcome at average 19.7 months follow-up (Fig. 3).



	LGI1 vs. NC						LGI1 vs. NON-LGI1						LGI1 vs. AD					
	Cut-off value	Se (%)	Sp (%)	J	LR+	LR-	Cut-off value	Se (%)	Sp (%)	J	LR+	LR-	Cut-off value	Se (%)	Sp (%)	J	LR+	LR-
P-SUVRg	1.21	92	100	0.92	∞	0.08	1.29	77	80	0.57	3.85	0.29	1.28	77	82	0.59	4.28	0.28
P/Th-ratio	1.32	77	100	0.77	∞	0.23	1.3	85	80	0.65	4.25	0.19	1.29	85	73	0.58	3.15	0.21
P/Mi-ratio	1.44	85	100	0.85	∞	0.15	1.45	85	93	0.78	12.14	0.16	1.46	85	100	0.85	∞	0.15

AD = Alzheimer's disease; AUC = area under curve; J = Youden Index (J = Sensitivity + Specificity -1); LGI1 = LGI1 autoimmune encephalitis; LR+ = positive likelihood ratio; LR- negative likelihood ratio; NC = negative controls; NON-LGI1 = non-LGI1 autoimmune encephalitis; P = putamen; ROC = receiver operating characteristic; Se = sensitivity; Sp = specificity; SUVRg = global brain normalized SUV-ratio; Th = thalamus

Figure 1

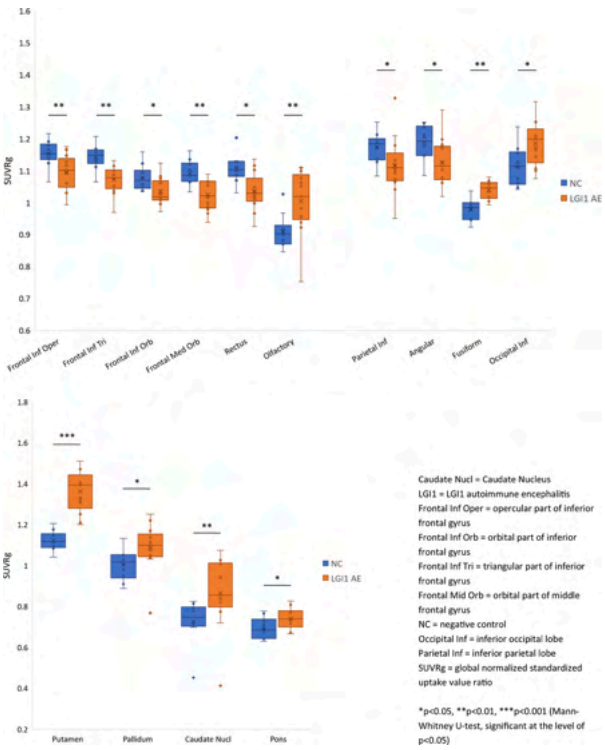
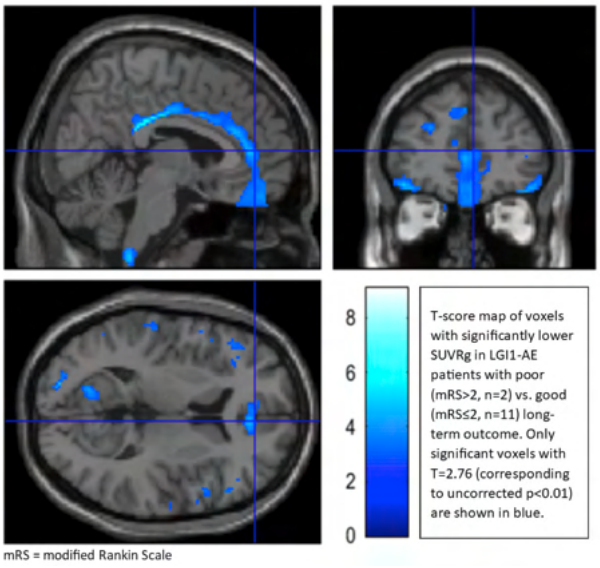


Figure 2



mRS = modified Rankin Scale

Figure 3

Conclusion: P/Mi and P-SUVRg can be used to aid in diagnosing LGI1-AE. Metabolic abnormalities in LGI1-AE extend beyond putamen and mediotemporal lobe into other subcortical and cortical regions. FDG-PET can aid in prognostication of LGI1-AE.

Disclosure: Nothing to disclose

OPR-022

Structural and functional cerebellar alterations in Parkinson's disease with postural instability and gait disorders

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Background and aims: This study aimed at assessing structural and functional cerebellar alterations in Parkinson's disease patients with postural instability and gait disorders (PD-PIGD).

Methods: 21 PD-PIGD patients and 23 age and sex-matched healthy controls underwent clinical, structural and functional MRI, including a motor-task (foot anti-phase movements) and a dual-task (foot anti-phase movements while counting backwards by threes). Local grey matter cerebellar volumes were evaluated automatically using an atlas propagation and label fusion strategy based on the freely available human cerebellum template and probabilistic atlas (SUIT). FMRI images were co-registered with structural images and fMRI analysis was focused on cerebellum.

Results: PD-PIGD patients showed reduced volume of left cerebellum lobules VI and X, right crus 1 and 2, bilateral lobules VIIb, VIIIa and vermis VIIb relative to healthy controls. During fMRI motor-task, PD-PIGD patients showed increased recruitment of right cerebellum crus 1 and bilateral crus 2 and a reduced activity of right cerebellum lobule VIIIa relative to healthy subjects. During fMRI dual-task, PD-PIGD patients showed increased activity of cerebellum crus 2 relative to healthy controls.

Conclusion: PD-PIGD patients showed reduced volumes in several cerebellar motor and non-motor areas relative to healthy controls. During both fMRI motor-task and dual-task, patients showed greater activation of cognitive cerebellar areas (crus 1-2) relative to healthy subjects and a reduced activity of a motor area (lobule VIIIb) during fMRI motor-task. The increased activity of non-motor cerebellar areas might be a consequence of grey matter atrophy or an attempt to compensate the functional failure of cerebellar motor areas.

Disclosure: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Neuroimmunology 1

OPR-023

New-onset status epilepticus caused by auto-immune encephalitis

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Background and aims: Auto-immune encephalitis is a severe, but curable, neurological disease. Many patients have fulminant seizures or status epilepticus (SE). The aim of this study was to describe the prevalence of an auto-immune aetiology of SE (AESE) and to identify factors pointing towards AESE.

Methods: In this prospective multicenter observational cohort study, adults were included with new-onset SE of unknown aetiology. At inclusion, patient- and SE characteristics were collected, and CSF was obtained. All samples were tested by immunohistochemistry and commercial cell-based assays. One year after inclusion, follow-up diagnoses were obtained and reviewed. Characteristics of patients with AESE were compared to the non-AESE patients.

Results: 50 patients were included with a median age of 57 years (IQR 47–72, range 23–86). 38% of the patients (n=19) had definite or probable AESE, of whom nine patients (18%) had neuronal antibodies (three anti-aminobutyric acid B receptor [GABABR], two N-methyl-D-aspartate receptor [NMDAR], two leucine-rich glioma-inactivated 1 [LGI1], 1 -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor [AMPAR], and one Glutamic-Acid-Decarboxylase 65 [GAD65]). The patients with definite or probable AESE were younger (p=0.040), more often had super-refractory SE (p=0.007), a systemic tumour (p=0.036), behavioral changes before SE (p=0.016), MRI hyperintensities temporal (p<0.0001), and pleocytosis in CSF (p<0.0001).

Conclusion: New-onset SE frequently has an auto-immune aetiology. Neuronal antibody testing should be performed routinely in all patients with SE with unknown aetiology. Additional to antibody testing, thorough evaluation of MRI and complete CSF evaluation seem useful to identify those with AESE.

Disclosure: Nothing to disclose.

OPR-024

Are there antibodies to neuronal surface antigens in patients with a clinical diagnosis of neurodegenerative disorder?

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Background and aims: Auto-immune encephalitis due to antibodies against neuronal surface antigens (NSA-Ab) frequently present with cognitive impairment, often as the first and prevalent manifestation, but few studies have systematically assessed the frequency of NSA-Ab in consecutive patients with established neurodegenerative disorders.

Methods: We studied sera of 93 patients (41F, 52M), aged 69.2±9.4 years, with neurodegenerative conditions, and of 50 population controls aged over 60 years. NSA-Ab were investigated by antigen-specific cell-based assays (CBAs). After testing, we evaluated the association between the NSA-Ab and clinical, CSF and radiological features.

Results: The patients included 13/93 (13.8%) who had specific NSA-Ab: Six GlyR, three GABAAR (1 also positive for AMPAR) two LGI1, one CASPR2 and one GABABR. One of the 50 controls (2%) was positive for NMDAR-Ab (p=0.20). No difference was observed in antibody frequency between patients presenting with parkinsonism and those presenting with dementia (p=0.55); however, NSA-Ab were more frequent in those with unclassified forms of dementia (5/13, 38.5%) than in those with unclassified parkinsonism (2/9, 22.2%) or classified forms of dementia (4/43, 9.3%) or parkinsonism (2/28, 7.1%) (p=0.03). A logistic regression analysis demonstrated that an unclassified diagnosis (p=0.02) and an irregular progression (p=0.024) were predictors of seropositive status.

Conclusion: NSA-Abs are relatively frequent in patients with neurodegenerative disorders, particularly in those with an irregular disease progression of atypical clinical features, inconsistent with a recognized diagnosis. The significance of these antibodies and their possible primary or secondary roles need to be investigated in prospective studies.

Disclosure: Nothing to disclose.

OPR-025

Seizure-related six homolog like two (SEZ6L2) auto-immunity: Neurologic syndrome and antibody effects

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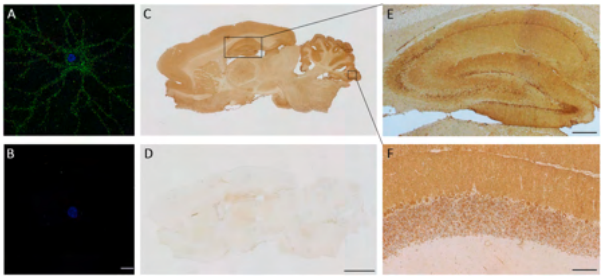
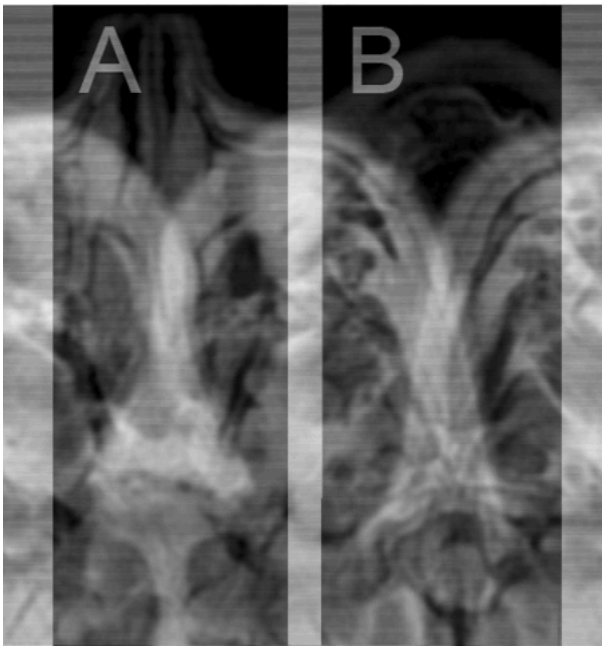
Background and aims: SEZ6L2 is a type 1 transmembrane protein highly expressed in the brain. We aim to describe the clinical syndrome of four new patients with SEZ6L2-ab, study the antibody characteristics, and evaluate their effects on neuronal cultures.

Methods: SEZ6L2-ab were initially identified in serum and CSF of a patient with cerebellar ataxia by immunohistochemistry on rat brain sections and immunoprecipitation from rat cerebellar neurons. We used a cell-based assay (CBA) of HEK293 cells transfected with SEZ6L2 to test the serum of 95 patients with unclassified neuropil antibodies, 331 with different neurological disorders, and 10 normal subjects. Additional studies included characterization of IgG subclasses and the effects of SEZ6L2-ab on cultures of rat hippocampal neurons.

Results: In addition to the index patient, SEZ6L2-ab were identified by CBA in 3/95 patients with unclassified neuropil antibodies but in none of the 341 controls. The median age of the four patients was 62 years (range: 54–69) and two were female. Patients presented with subacute gait ataxia, dysarthria and mild extrapyramidal symptoms. Initial brain MRI was normal and CSF pleocytosis was found in only one patient. None improved with immunotherapy. SEZ6L2-ab recognized conformational epitopes. IgG4 SEZ6L2-abs was found in all four patients, and it was the predominant subclass in 2. SEZ6L2-abs did not alter the number of total or synaptic SEZ6L2 or GluA1 clusters on the surface of hippocampal neurons.



Immunoreactivity of SEZ6L2-ab in hippocampal neurons and rat brain sections.



Initial and follow-up brain MRI of patient 2

Conclusion: SEZ6L2-ab associate with a subacute cerebellar syndrome with frequent extrapyramidal symptoms. The potential pathogenic effect of the antibodies is not mediated by internalization of the antigen.

Disclosure: No disclosures.

OPR-026

Safety and tolerability of efgartigimod in patients with generalized myasthenia gravis: phase 3 adapt study results

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Background and aims: Efgartigimod, a human IgG1 antibody Fc-fragment, blocks the neonatal Fc receptor, which decreases recycling of IgG and reduces pathogenic autoantibody levels. In a phase 2 study, it demonstrated efficacy and was well tolerated in patients with generalized myasthenia gravis (gMG), an IgG antibody-mediated disease.

Methods: ADAPT was a phase 3, randomized, double-blind, placebo controlled, global, multicenter 26-week study that evaluated the safety and efficacy of efgartigimod in patients with gMG. Participants were randomized 1:1 to receive four weekly 10mg/kg infusions of efgartigimod or placebo with subsequent treatment cycles administered according to clinical response.

Results: 167 (129 AChR-Ab+ and 38 AChR-Ab-) patients were randomized. Significantly more patients treated with efgartigimod, compared to placebo, achieved sustained statistically and clinically significant improvement in both MG-ADL and QMG scores. The majority of adverse events (AEs) were mild or moderate. Infections were of special interest and occurred with similar frequency in efgartigimod and placebo treated patients (46.4% and 37.3%, respectively). The type and severity of infections were similar between groups, with no serious or opportunistic infections in the efgartigimod group. Headache was the most common AE (efgartigimod: 28.6%, placebo: 27.7%), but none were serious or required treatment interruption. Most patients experienced headache only once. Infusion related reactions were infrequent, despite the absence of premedication, occurring in 3.6% of efgartigimod and 9.6% of placebo patients, none were serious or required a change in efgartigimod dose and no hypersensitivity or anaphylactic reactions were reported.

Conclusion: Efgartigimod was well tolerated and clinically efficacious in patients with gMG.

Disclosure: The ADAPT study was funded by argenx.

Neuroepidemiology

OPR-027

A nationwide study of the incidence, prevalence and mortality of Parkinson's disease in the Norwegian population

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Background and aims: Epidemiological studies of Parkinson's disease (PD) show variable and partially conflicting findings with regard to incidence, prevalence and mortality. These differences are commonly attributed to technical and methodological factors, including small sample sizes, differences in diagnostic practices, and population heterogeneity. We aimed to determine the nationwide incidence, prevalence and mortality of PD in the Norwegian population.

Methods: We used the Norwegian Prescription Database, a population-based registry of drug prescriptions dispensed from Norwegian pharmacies, to assess the incidence, prevalence and mortality of PD over the period 2004-2017. PD diagnosis was defined by proxy, based on the prescription dopaminergic drugs over a continuous time. In total, 13,053 male- and 10,143 female-PD patients were identified.

Results: PD incidence and prevalence increased with age, peaking at 85 years (Fig. 1). The male/female prevalence ratio was 1.5 across all ages, but the incidence ratio increased with age, from 1.4 in those <60 years, to 2.03 among those >90 years. PD prevalence increased during the observation time, with larger changes observed in the older age groups. While in all ages, mortality was higher in PD compared to the general population, PD mortality odds ratios decreased with age, approaching 1.0 among individuals >90 years old, and were generally higher in females than in males (See Fig. 2 & Fig. 3).

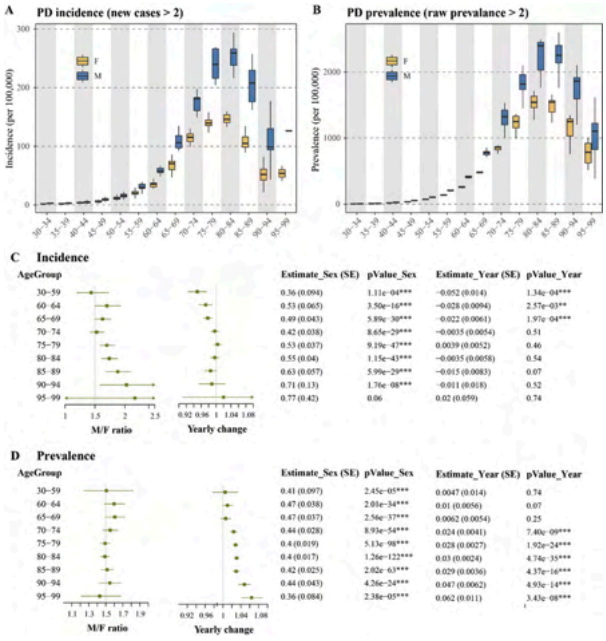


Fig. 1 Incidence and prevalence of PD in the Norwegian population during 2005–2016; (A,B) Incidence and prevalence, (C,D) The impact of the time period and sex were assed individually for each age group

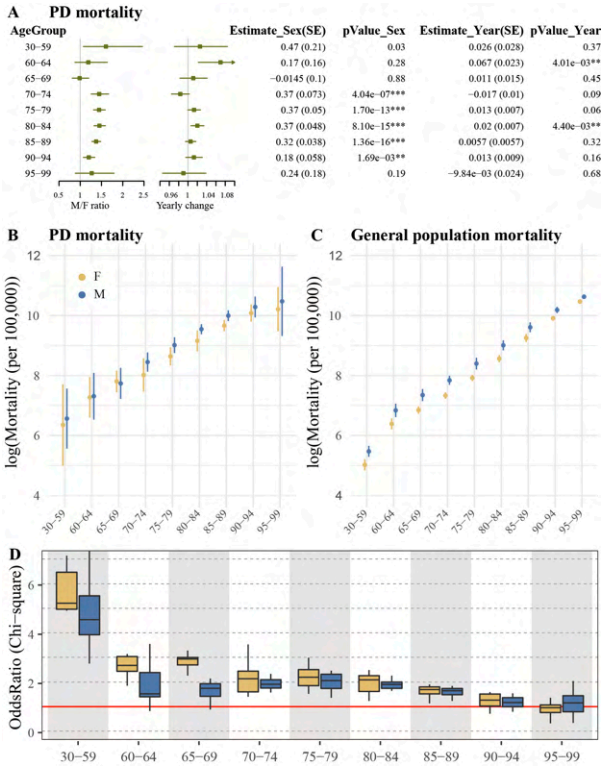
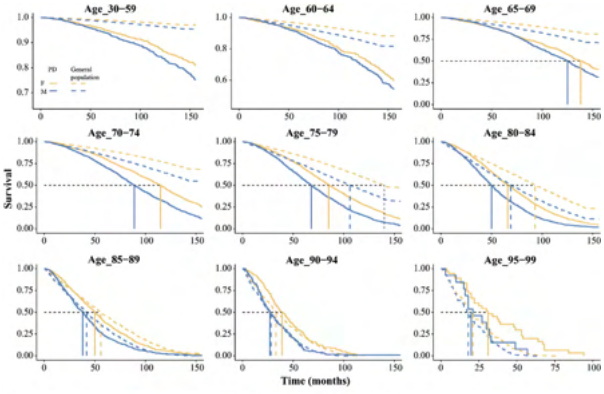


Fig. 2 Mortality of PD in the Norwegian population during 2005-2016; (A) The impact of the time period and sex on PD mortality, . (B,C) Mortality per 100,000 person-years in PD , (D). Death odds ratio



		Time (month) to 50% survival							
		30-59	60-64	65-69	70-74	75-79	80-84	85-89	90-94	95-99
General population	Male	> 156	> 156	> 156	> 156	106	70	42	28	18
	Female	> 156	> 156	> 156	> 156	140	93	56	33	20
PD	Male	> 156	> 156	125	89	68	50	38	27	21
	Female	> 156	> 156	138	115	85	66	50	39	31

Fig. 3 Kaplan Meier survival analysis showing sex differences

Conclusion: PD epidemiology, including sex-differences, is extremely dynamic and is highly age and time-period dependent. Sex differences in PD mortality are unlikely to stem from disease-specific negative impact of survival in males.

Disclosure: No disclosures

OPR-028

Phantom menace: the risk of low polio vaccine coverage in Brazil – a cross-sectional study

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[1] *Faculty of Medicine, Federal University of Goiás, Goiânia, Brazil*

Background and aims: Poliomyelitis (PM) is a viral infectious disease that affects CNS by causing acute flaccid paralysis and has been eradicated from Brazil. However, given the reduction in vaccination coverage (VC), we aim to analyze this new scenario, especially the pandemic effects on 2020 data.
Methods: This is a cross-sectional study with information from Brazil's Information System from the Immunization Nacional Program about poliomyelitis (ICD10-A80), described as "poliomelite" or "poliomelite 4 anos", involving data from January 2010 to December 2020.
Results: We identified that the best campaign years were in 2011 (101.33%) and 2013 (100.71%). However, the coverage of 80%, WHO's recommendation for herd immunity, is not achieved since 2016. In 2020, four out of the five Brazilian regions had their worst vaccination rate in the decade and only the southern region figured over 80%. As such, the regional disparity is visible: the North had 54.64% of vaccination coverage in 2020, while the South obtained 84.84%. Further, we found that immunization against PM, in a national perspective, is presenting a downward trend (APC=-3,88%;CI 95%=-5,2%;-2,6%).

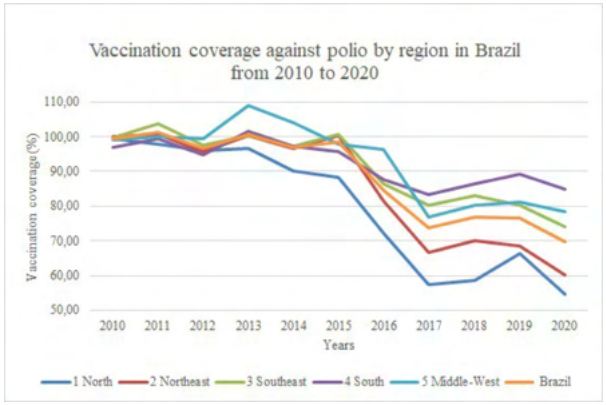

Fig. 1: Temporal analysis of polio vaccination coverage by Brazilian regions.

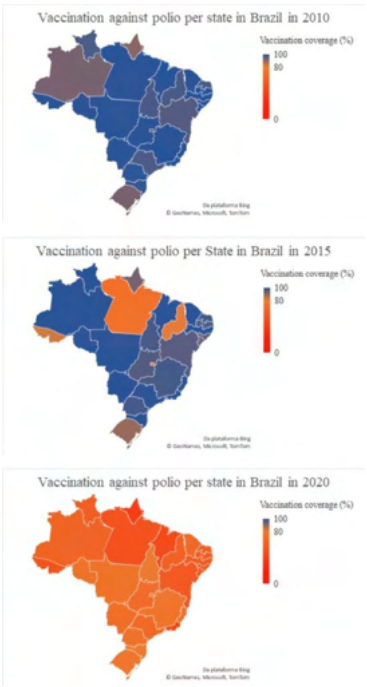

Fig. 2: Evolution of the polio vaccination rate in Brazilian states over time. States colored orange or red have not reached the WHO recommended vaccination rate.

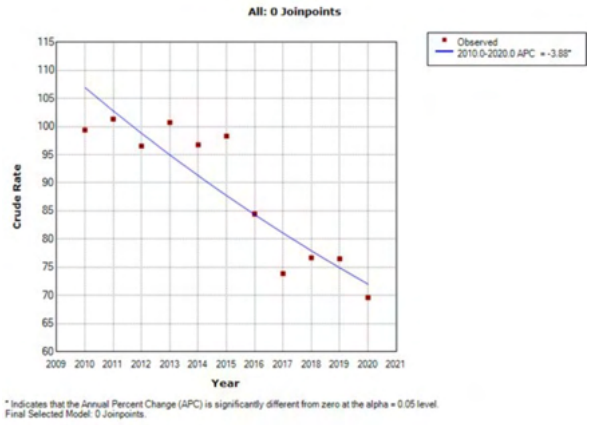

Fig. 3: Trend curve of polio vaccination rate behavior over the past decade.

Conclusion: We provide worrying information about immunization against PM in Brazil as our national health system (and neurology services) are not prepared to fight this disease, eradicated in 1989.
Disclosure: Nothing to disclose.

OPR-029

Meningitis in the 21th century – A cross-sectional study from brazilian healthcare database

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Background and aims: Multifactorial Meningitis (MM) is a group of diseases of compulsory notification in Brazil, defined by inflammation of the meninges due to viral, fungal, or bacterial agents. We aim to investigate the epidemiological rates of these diseases in the country.

Methods: We gathered information about MM (ICD10 – G00/A39/A87) from Brazil's Information System for Notifiable Diseases (SINAN), including data from January 2001 to June 2020. Population data were collected from the Brazilian Institute of Geography and Statistics (IBGE).

Results: We identified 432,426 cases of meningitis, among which 43,888 (10.2%) died. The general incidence was 11.2 cases/100,000 hab. (95%CI: 10.69–11.70; SD=3.85). The mean lethality of the disease was 10.15% (95%CI: 10.06–10.2). The average mortality was 11.44 per million (95%CI: 10.77–12.10; SD: 5.11). Individuals aged 80 or over had the highest lethality: 33.44% (95%CI: 31.61–35.32); while children aged 5–9 years had the lowest rate: 3.58% (95%CI: 3.45–3.71). We also observed a downward trend (APC= -1,91%; CI95%=-3,3%; -0,5%) in the lethality curve of MM in Brazil.

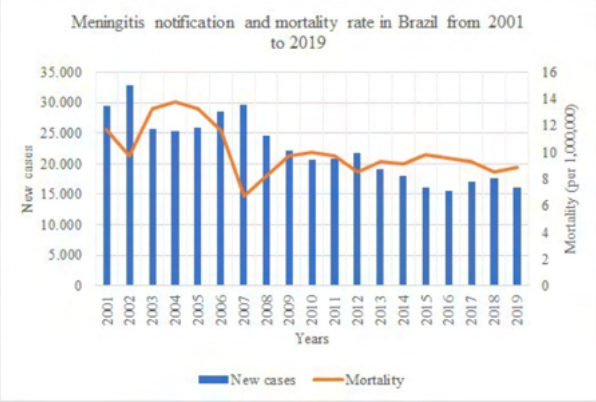

Fig. 1: Incidence and mortality of MM over time in Brazil.

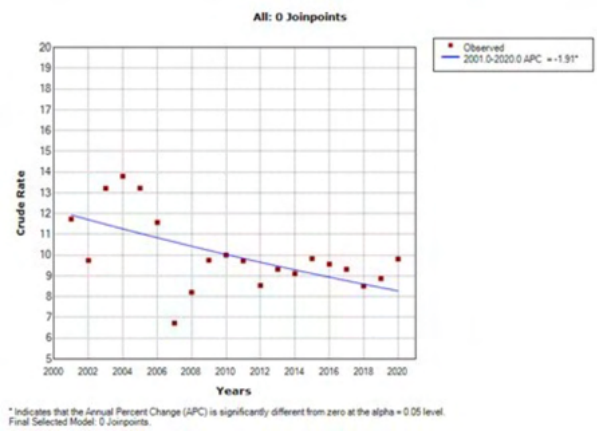

Fig. 2: Trend curve of MM lethality over time.

Fig. 3: The behavior of the MM lethality with aging.

Conclusion: The study reveals a notorious incidence of MM in Brazil. However, the lethality trend has been downward in this century, which may be an effect of improving health care and the epidemiological surveillance system for infectious diseases. Furthermore, special attention to the elderly is crucial in these cases as a higher lethality rate is found among this group.

Disclosure: Nothing to disclose.

OPR-030

Prevalence, incidence, and characteristics of narcolepsy patients in Germany – A population-representative study

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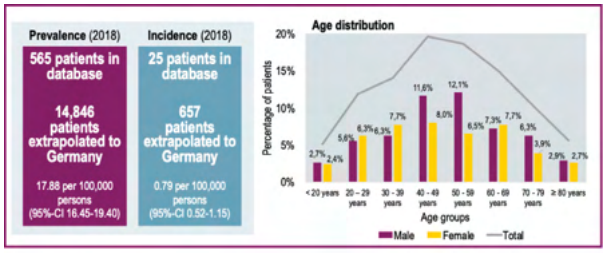
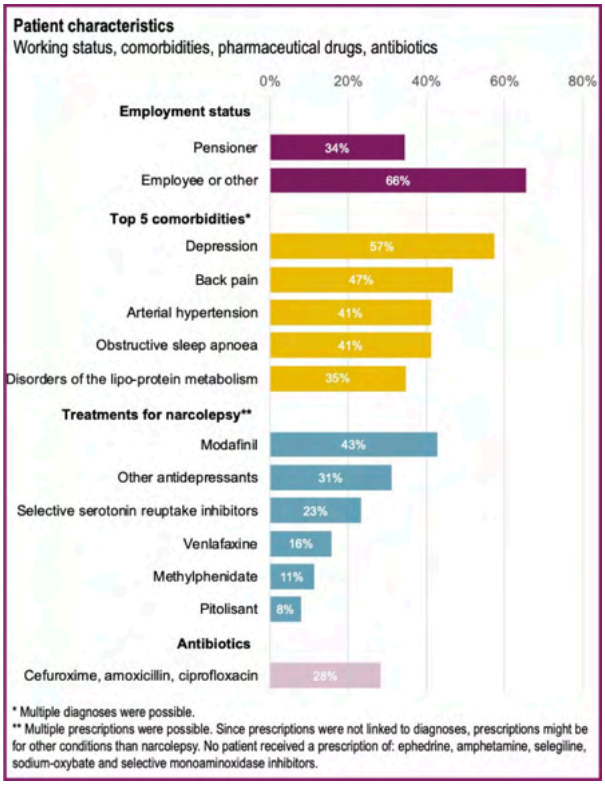
Background and aims: Previous studies estimated a prevalence of 47 narcolepsy patients per 100,000 persons in Europe and yearly incidence of 0.64–1.37 per 100,000. Epidemiological information for narcolepsy is limited, therefore this study aimed to estimate diagnostic prevalence and incidence and to describe narcolepsy patient characteristics in Germany.

Methods: This study used the InGef research database, an anonymized representative dataset of four million persons covered by statutory health insurance in Germany, adjusted to the age/gender distribution of the German population. Patients with confirmed narcolepsy diagnoses in 2018 (using ICD-10 codes) were included. Mid-p exact tests were used to calculate 95% confidence intervals (CIs). Patients with narcolepsy diagnoses and narcolepsy-targeting therapy in 2014–2018 were included to describe resource use in the year prior to diagnosis.

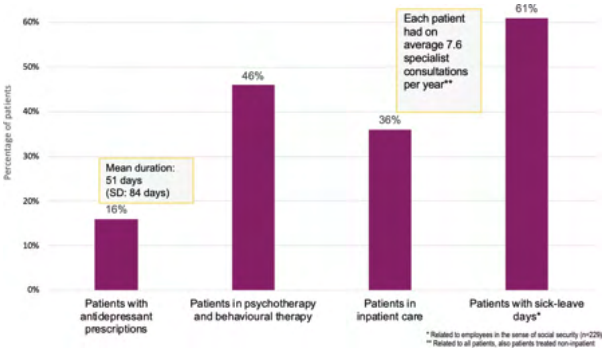
Results: In 2018, per 100,000 persons, diagnostic prevalence was estimated as 17.88 (95%-CI 16.45–19.40), and 12-month incidence as 0.79 (0.52–1.15). Patient characteristics are shown in Figure 2. 46% patients were in psycho-behavioural therapeutic treatment and 61% of employees had sick-leave days (Figure 3). 28% received antibiotics compared to 20% in the general population.



Incidence, prevalence and age distribution of narcolepsy in Germany



Patients characteristics 2013–2018



Health-care resource use in the year prior to narcolepsy diagnosis 2013–2018

Conclusion: Diagnostic prevalence was lower and incidence consistent with previous reports, though previous estimates may diverge in terms of age/gender-distributions. Patients showed a significant utilization of the health resources, incl. sick-leave days. Almost half of the patients underwent psycho-behavioural treatment in the year prior to diagnosis, which might indicate high burden of mental disease or an incorrect referral due to lack of symptom recognition. The increased use of antibiotics could indicate more frequent infections than in the general population.

Disclosure: This study was financially supported by Jazz Pharmaceuticals

Neurorehabilitation

OPR-031

Assessing communicative abilities in patients with severe acquired brain injury by Functional Communication Measures.

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Background and aims: The assessment of communicative abilities in patients with acquired brain injury (ABI) is challenging, especially in patients emerging from Minimally Conscious State (eMCS). The Functional Communication Measures (FCMs) assess communicative and swallowing abilities on a one (least functional) to seven (most functional) scale in collaborative patients with brain injury (Mullen, 2004). The present pilot study aimed at evaluating 1. the inter-rater agreement of an Italian short version of FCMs in a cohort of patients with severe ABI; 2. the usefulness of FCMs in profiling patients emerging from Disorder of Consciousness.
Methods: Aim 1: The Italian version of short FCMs including seven items (attention, memory, augmentative-alternative communication, motor speech, spoken language comprehension and expression, swallowing) was blindly administered by two speech-therapists to eight conscious patients with sABI (two females; mean age=63.4±17.2 years, mean Level of Cognitive Functioning=6.5±1.4). The inter-rater reliability was calculated for each FCMs scale. Aim 2: Two patients in eMCS (both females, 74- and 64-year-old) were evaluated by short FCMs, Coma Recovery Scale Revised (CRS-R) and Disability Rating Scale (DRS).
Results: Inter-rater agreement was very high for swallowing and attention scales, and moderate or substantial for the remaining items. The two eMCS patients showed the same DRS-R and CRS-R total scores, and yet the FMCs scales attention, swallowing, motor-speech and spoken language expression revealed different functional communication abilities.
Conclusion: This pilot study showed a good inter-rater reliability of the Italian version of FCMs. This clinical tool seems to allow fine-grained characterization of patients' cognitive abilities.
Disclosure: The authors reports no disclosures.

OPR-032

Multicentre longitudinal study on predictors of long-term mortality in Disorders of Consciousness

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Background and aims: The 12-month mortality rate of patients with prolonged Disorders of Consciousness (DoC) is high (approximately 48%) due to high risk for severe medical complications. The present international multicentre longitudinal study, performed by the Special Interest Group on DoC of the International Brain Injury Association, aimed at identifying predictors, easy to collect at the bedside, for long-term outcome including mortality.
Methods: 12 specialized centres enrolled patients in Vegetative (VS) or in Minimally Conscious State (MCS) within three months from acquired brain injury. Demographic, anamnestic, clinical, and neurophysiologic data were collected at enrolment; patients were followed up to 24 months post-injury.
Results: From a consecutive sample of 147 patients with DoC, data on mortality were available for 143 traumatic (n=55) and non-traumatic (n=88) patients (VS=68, 19 females; mean age=51.1±19.5; MCS=75, 22 females; mean age=46.8±20.0). Within 24 months after brain injury, 41/143 patients (28.7%) died. Mortality rate was higher in VS (42.6%) than in MCS (16%; $p<0.001$). Multivariate regression showed that significant predictors of mortality were older age and lower Coma Recovery Scale-Revised total score in the VS group, and female sex and absence of alpha rhythm on EEG in the MCS group.
Conclusion: The present longitudinal study demonstrated that lower level of consciousness (as measured by CRS-R total score), older age, female sex, and alteration of thalamocortical connections (as evaluated by conventional EEG) at enrolment were independent predictors of long-term mortality. These multimodal bedside findings can help clinicians and families navigate the complex clinical decision-making process.
Disclosure: The authors report no disclosures.

OPR-033

Bilateral sequential TBS in rehabilitation of post-stroke hemiparesis – feasibility and safety study

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Background and aims: We previously showed that bilateral sequential stimulation consisting of stimulation of the non-dominant M1 with an excitatory protocol preceded by the inhibitory one over dominant M1 with theta-burst stimulation (TBS) can improve motor skill learning in healthy participants. This study's aim was to check whether a similar approach would be suitable for use in the rehabilitation of post-stroke hemiparesis.
Methods: 10 patients (mean age 58 years [range 38–69]) with hemiparesis due to MCI stroke, in the subacute post-stroke recovery phase, were enrolled in the study. They all had daily physio and occupational therapy for four weeks. During the 1st and 2nd week, bilateral sequential TBS was delivered (using standard cTBS and iTBS protocols) each day before therapy procedures. Hand tapping (HT), simple reaction time (RT), and the Purdue peg-board task (PPT) were measured, for each hand, before therapy, after the first and the second week, after the end of therapy (4th week), and a month following completion of the therapy.
Results: Healthy hand showed clear improvement with time, consistent with the learning/training effect of repeated practice. Paretic hand showed significant improvement in HT, while RT showed variable results. No adverse effects were reported apart from an occasional mild headache at the area of the coil contact with the scalp.
Conclusion: Bilateral sequential TBS is feasible for use to boost the effectiveness of physio and occupational therapy in subacute post-stroke hemiparesis. There seem to have no major safety issues and no untoward effects on the healthy hand. Further control studies are needed.
Disclosure: This study was supported by the Ministry for Education, Science and Technological Development of Republic of Serbia [grant number 175012].

OPR-034

EFFECTIVENESS OF A COGNITIVE REHABILITATION PROGRAM IN PATIENTS WITH ULTIPLE SCLEROSIS (MS)

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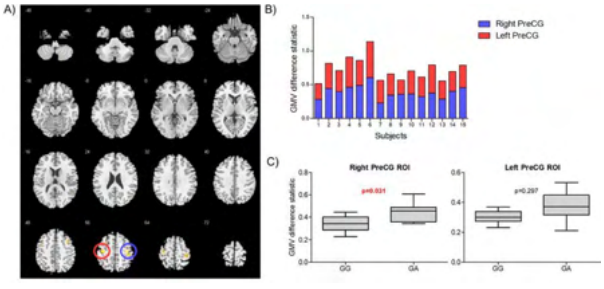
Background and aims: Cognitive rehabilitation is an approach to improve the functional status of multiple sclerosis (MS) patients. Specifically, cognitive rehabilitation using virtual tools has been supported by neuroimaging findings, where an increase in grey matter volume (GMV) and cognitive improvement after therapy have been reported.
Methods: Prospective observational study designed to identify the effectiveness of a cognitive rehabilitation (with NeuronUP online tool) and their associated functional and structural changes in Magnetic Resonance Image (MRI) studies in MS patients. Fifteen patients with MS were included (age=43.76; 11 women). Time of disease evolution = 10.6 years; Expanded Disability Status Scale=2.75. Three sessions (for 45 minutes) a week were planned during eight consecutive weeks. The rehabilitation program was focused on: attention, processing speed, memory, language, executive functions, visuospatial ability and social cognition. A neuropsychological evaluation and a functional MRI were performed before and after intervention.
Results: Significant improvements in inmediate verbal memory (p=0.017), delayed visual memory (p=0,009), working memory (p=0,001) and verbal semantic fluency (p=0.012) were observed. Subjective perception of cognitive status improved too (p=0.004). Patients showed a significant increase of GMV after the cognitive rehabilitation program in frontal, parietal, temporal lobes, and cerebellum. The most significant increase was inthe primary motor cortex of both hemispheres. GMV differences were also shown at premotor regions of both hemispheres.



Changes of grey matter volume (GMV) after the cognitive rehabilitation program.

Conclusion: Cognitive treatment is an effective approach to improve cognitive status in MS and can induce changes in cortical reorganization, which will help to improve either cognitive or brain reserve.
Disclosure: No disclosure to declare.

OPR-035

Apomorphine therapy for patients with chronic disorders of consciousness: a multimodal open-label study

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Background and aims: Apomorphine, a repurposed dopaminergic drug, is a promising therapy to improve the recovery of patients with disorders of consciousness (DOC), with a postulated action on the mesocircuit. This prospective open-label study aimed to confirm preliminary results on clinical efficacy and investigate its action on brain function.
Methods: Six patients with chronic DOC (four male, four traumatic, 38.8 year-old average, 99 days post-onset average) received daily subcutaneous apomorphine therapy for 30 days. Multimodal monitoring was performed from 30 days before to 30 days after treatment. Outcome measures included repeated behavioural scales, high-density electroencephalography (hdEEG) and positron emission tomography (PET).
Results: Compared to baseline, three patients improved their behavioural diagnosis during treatment, two additional patients improved during the 12-month follow-up and the last patient emerged before treatment start but improved on all rehabilitation scales during treatment. Mean Coma Recovery Scale-Revised scores improved during treatment (2.1 points) and 30-day washout (5.2 points) periods, compared to baseline (Table 1). Healthcare staff and family rated the patient's clinical condition 20.5% and 30.9% better after treatment, respectively (Table 2). Alpha-band hdEEG functional connectivity measured by network centrality increased by 13.6% on average after treatment (Fig. 1). Wholebrain fluorodeoxyglucose metabolism increased by 12.4% on average between PET before and after treatment.

Patient	Aetiology	Time since injury	Outcome measure	Inpatient phase			Follow-up		
				Baseline 30 days	Treatment 30 days	Washout 30 days	6 months	12 months	24 months
P1	Haemorrhage	3.4 months	Mean CRS-R score (0-23)	5,6	8,0	8,8			
			Most frequent diagnosis	UWS	MCS-	MCS-			
			Final clinical diagnosis	MCS-	MCS+	MCS+	MCS+	dead	dead
P2	Traumatic brain injury	4.7 months	Mean CRS-R score (0-23)	9,1	9,3	10,6			
			Most frequent diagnosis	MCS-	MCS-	MCS-			
			Final clinical diagnosis	MCS-	MCS-	MCS-	MCS-	EMCS	EMCS
P3	Traumatic brain injury	3.0 months	Mean CRS-R score (0-23)	17,3	19,7	22,0			
			Most frequent diagnosis	MCS+	EMCS	EMCS			
			Final clinical diagnosis	MCS+	EMCS	EMCS	EMCS	EMCS	
P4	Traumatic brain injury	2.0 months	Mean CRS-R score (0-23)	13,9	12,7	20,2			
			Most frequent diagnosis	MCS+	MCS+	EMCS			
			Final clinical diagnosis	EMCS	EMCS	EMCS	EMCS	EMCS	
P5	Haemorrhage	3.2 months	Mean CRS-R score (0-23)	7,9	8,8	9,6			
			Most frequent diagnosis	MCS-	MCS-	MCS-			
			Final clinical diagnosis	MCS-	MCS-	MCS-	MCS+		
P6	Traumatic brain injury	3.3 months	Mean CRS-R score (0-23)	3,2	11,2	17,0			
			Most frequent diagnosis	UWS	MCS+	MCS+			
			Final clinical diagnosis	UWS	MCS+	MCS+			

Table 1. Coma Recovery Scale – Revised (CRS-R) results. Demographics, mean CRS-R total scores, most frequently observed diagnoses and final clinical diagnoses for 30-day inpatient periods, as well as clinical diagnoses during follow-up when available.

Question (% of maximum)	BEFORE (mean)		AFTER (mean)		DIFFERENCE BEFORE-AFTER	
	Staff	Family	Staff	Family	Staff	Family
Presence	38,9	37,4	63,6	69,7	+24,7	+32,3
Verbal comprehension	31,8	32,9	57,1	68,2	+25,3	+35,3
Communication	21,8	24,6	48,6	68,3	+26,8	+43,7
Spontaneous motricity	29,0	28,5	57,7	60,0	+28,7	+31,5
Voluntary motricity	27,9	22,6	44,9	53,3	+17,0	+30,7
Comfort	49,4	49,1	65,0	71,3	+15,6	+22,2
Arousal	56,5	55,4	71,5	72,9	+15,0	+17,4
Emotions	46,5	40,8	57,3	75,2	+10,8	+34,4
Treatment effect			70,1	53,8		
Treatment tolerance			72,0	79,7		
Mean for all questions	37,7	36,4	60,8	67,2	+20,5	+30,9

Table 2. Caregivers' questionnaire. Rating of the patient's clinical condition by three members of the clinical staff and by the patient's family, assessed immediately before and one week after the end of apomorphine treatment.

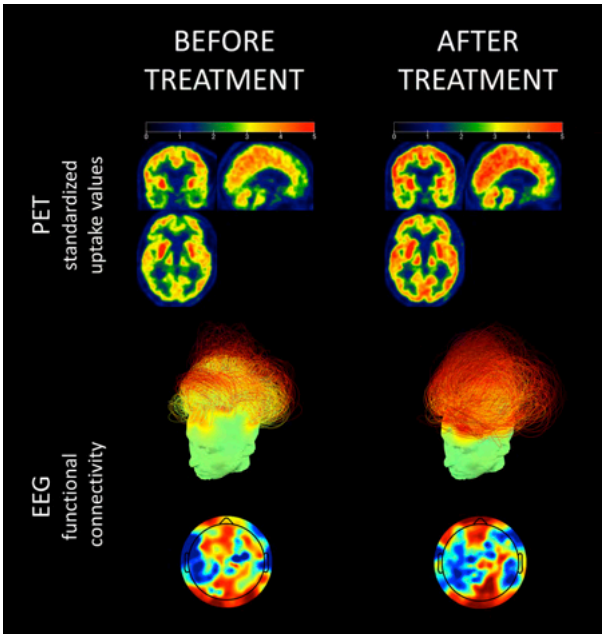

Fig. 1. Positron emission tomography (PET) and electroencephalography (EEG). Wholebrain metabolism in a representative patient (P6; top row), topographs of mean alpha-band networks (middle row) and alpha participation coefficient maps (lower row).

Conclusion: Multimodal improvements were observed in chronic DOC patients after a 30-day treatment regimen with apomorphine. These results suggest a beneficial action on consciousness that is associated with increased brain connectivity and metabolism. These results will need to be confirmed in a subsequent multicentre randomized placebo-controlled trial (EudraCT:2018-003144-23; Clinicaltrials.gov:NCT03623828).
Disclosure: We thank the University and Hospital of Liège, the Belgian National Fund for Scientific Research (grants to LS, NL, OG, SL), NeuroHealing Pharmaceuticals, the Fund Generet of the King Baudouin Foundation, all patients and their families.

Miscellaneous: Neuro-ophthalmology/ neuro-otology and the arts

OPR-036

Sonic Support Group: releasing the therapeutic potential of art for NHS staff and frontline workers.

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Background and aims: The COVID-19 pandemic is putting exceptional emotional strain on frontline workers while severely restricting their opportunities to maintain their wellbeing, including access to art. This is a joint initiative between Neurofringe – a group of UK neurologists interested in the intersections of neuroscience, art and society – and London-based artist Abbas Zahedi.
Methods: The Sonic Support Group pilot is aimed at frontline workers and NHS staff. Keyworkers are granted access to Zahedi's currently dormant exhibition, Ouranophobia SW3, providing them with a moment of respite from their work. This re-presentation of Ouranophobia SW3 for frontline staff is made possible under government guidance for hosting physical support groups. To minimise risk, access to the space is limited to single visitors at any one time. Amendments to safety measures are considered in line with Government guidance.
Results: Ouranophobia SW3 contains site-specific sound and physical art works, situated within a disused sorting office in Chelsea (South-West London). Elements of the exhibition relate to Zahedi's own experiences exploring themes of grief, loss and sensory deprivation – aspects of reality we now face on an unprecedented scale. The 'thera-poetic' potential of the exhibition within the physicality of the site provides a framework through which the escalating levels of workplace trauma we are seeing today can begin to be alleviated.
Conclusion: The Sonic Support Group intends to highlight the essential capacity for care that is present in art and to become a catalyst towards reimagining what it means to support one another in times of need.
Disclosure: Nothing to disclose.

OPR-037

Convergence spasm: a clinical and video-oculographic series of 12 patients

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Background and aims: Convergence spasm (CS) is mostly a non-organic disorder featuring intermittent episodes of convergence, accommodation and miosis. There are few studies assessing CS patients, and formal recording is lacking. This study aims to summarize CS clinical features, mimickers, and outcome, and to provide infrared pupilography (IP) data in a group of patients.
Methods: A retrospective analysis of CS cases referred to our neuro-ophthalmology clinic from 2014 to 2020 was performed.
Results: A total of 12 (83% female; mean age onset of symptoms, 37.3±16.0 years-old) cases were collected. There was history of depression and functional disorder in 50% and 41.7% patients, respectively. Main presentation was intermittent diplopia (91.7%). Diagnostic possibilities on referral included sixth nerve palsy (6NP) (41.7%), internuclear ophthalmoplegia (INO) (33.3%), myasthenia gravis (16.7%) and neuromyotonia (16.7%). Organicity had been ruled out. CS diagnosis was made in average 27.6±53.5 months after initial medical encounter. IP was performed in eight patients. In all except one patient, convergence preceded miosis by around 260 (range 100–600) milliseconds. In 33.3% patients CS episodes were spontaneous while in 66.7% were triggered by lateral versions. Abduction pseudo-limitation and abducting nystagmus were present in 25.0% and 37.5% patients, respectively. Apart from reassurement, treatment was needed in 50%. Improvement was noted in 50% of those treated.
Conclusion: CS commonly mimics neurologic disorders, including 6NP and INO, explaining diagnosis delay in our series. Eye recording showing evidence of convergence preceding miosis might be useful in difficult cases. Spontaneous resolution is possible, but targeted therapies are needed in 50% of patients.
Disclosure: No disclosures.

OPR-038

Longitudinal whole-brain metabolic network changes following acute unilateral vestibulopathy

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Background and aims: Symptoms of acute unilateral vestibulopathy (AUV) partially recover due to adaptive brain plasticity. In this study, we analysed whole-brain metabolic connectivity changes after AUV by longitudinal 18F-FDG-PET imaging.
Methods: 22 patients with AUV underwent resting state 18F-FDG-PET scans in the acute phase (mean: 6d) and after partial behavioural compensation (mean: 6m). PET data were compared to 22 matched controls. Images were flipped, reconstructed, registered, filtered, normalized, and segmented (AAL2/3 atlas). Pearson's correlations between all segmented brain regions were performed ($r>0.5$/ $p<0.001$). Functional metabolic connections between and within hemispheres, and in vestibular/multisensory/motor/ cognitive networks were calculated.
Results: Patients had severe vestibular asymmetry in the acute stage (mean horizontal slow-phase velocity (SPV): 9.9°/sec, subjective visual vertical (SVV): 7.6°), which recovered until 6m after AUV (SPV: 0.7°/sec, SVV: 1.7°). As compared to controls, whole-brain metabolic network analysis indicated a significant drop in the total number of connections (830 vs. 440), and specifically in interhemispheric projections between homotopic multisensory regions in the acute stage. In the chronic stage, the asymmetry in interhemispheric connections of homotopic regions persisted. Multisensory network connectivity relatively increased in the ipsilesional hemisphere compared to the early stage. Patients with a persistent caloric vestibular deficit had a higher asymmetry index compared to those with reconstituted peripheral function.
Conclusion: AUV disrupts the symmetry of multisensory metabolic networks between hemispheres persistently and mostly in patients with a chronic peripheral vestibular deficit. These data may be important for the understanding of higher sensory network dysfunction and conversion risk to functional dizziness after AUV.
Disclosure: Nothing to disclose.

OPR-039

Novel diagnostic index test CATCH2 improves detection of acute vestibular stroke (EMVERT study)

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Background and aims: Patients with acute vertigo and dizziness account for about 4% of all visits in the emergency department (ED). Stroke is the underlying cause in 4-15%. About 10% of all vestibular strokes are missed at first contact. Therefore, improvement of the diagnostic algorithms is urgently needed.
Methods: 410 consecutive patients with acute vertigo, dizziness or imbalance were included in the prospective EMVERT study in the ED of a university hospital (LMU Munich). All patients underwent a structured history taking, clinical neurological exam and neurophysiological assessment (including videooculography, mobile posturography) in the ED. A cranial MRI was performed within seven days to detect stroke. Post-hoc analysis identified factors, which had the highest accuracy to indicate vestibular stroke in the acute setting.
Results: A novel diagnostic index test, called CATCH2, was composed, which included the following features: C – central clinical signs and symptoms (e.g. dysarthria, hemiataxia), A – age >60 years, T – triggers absent, C – cover test with skew deviation, H – head impulse test normal, H – history of vertigo or dizziness absent. Each feature was weighted with one point, if present. For sum values of four of six points, the AUC to detect vestibular stroke was 0.90, the sensitivity 91% and specificity 87%. CATCH2 outperformed ABCD2 (sensitivity: 64%, specificity: 53%) and HINTS (sensitivity: 86%, specificity: 36%).
Conclusion: CATCH2 is a reliable and clinically feasible diagnostic index test to detect acute vestibular stroke in patients with different presentations of vertigo and dizziness (including those without spontaneous nystagmus.
Disclosure: No disclosures.

OPR-198

Biallelic variants in the molecular chaperone DNAJB4 are a genetic cause of myopathy with respiratory muscle involvement

C. Domínguez-González [1], M. Mroczek [2], S. Kapetanovic [3], A. AlSaman [4], R. Gogoi [5], R. Charlton [6], A. Topf [5], A. Hernández-Laín [1], M. Olivé [7], N. Laing [8], G. Ravenscroft [8], S. Beecroft [8], H. Goullee [8], R. Barresi [6], V. Straub [9]

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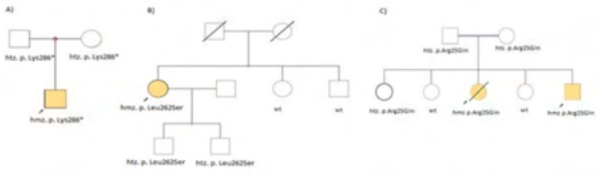
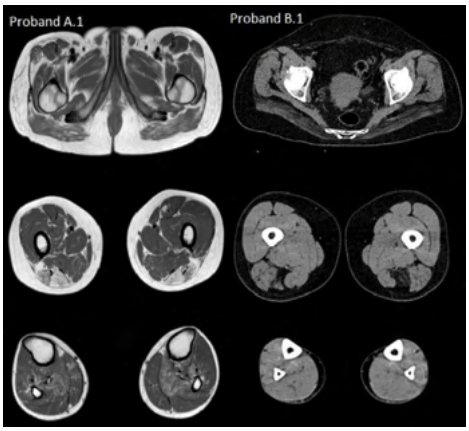
Background and aims: DNAJB4 is a molecular chaperone and member of the heat shock protein family. It was identified as a tumour suppressor gene and is associated with prolonged survival in lung cancer.

Methods: We have screened our database of >2,000 exomes of patients with neuromuscular disorders and identified two patients with likely pathogenic variants in DNAJB4. Family C was found through international collaboration.

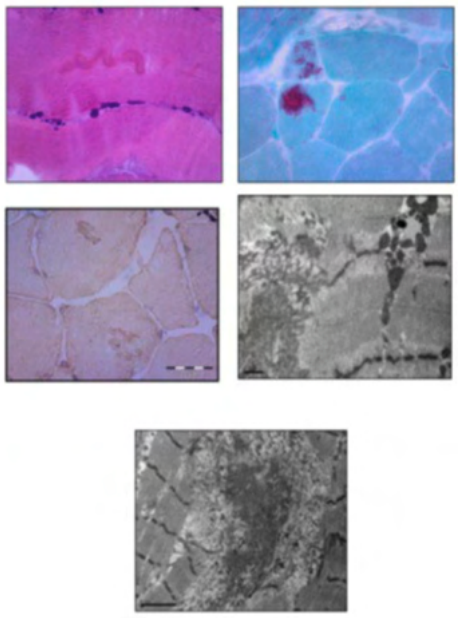
Results: We identified four individuals from three unrelated families with severe diaphragmatic weakness diagnosed after the development of acute respiratory failure, which led to permanent mechanical ventilation. All had no apparent muscle involvement at the time of diagnosis, but they did have some degree of spinal rigidity. One of the patients died at 11 due to respiratory insufficiency. CK levels were normal. Muscle MRI of two probands showed a similar selective involvement of semitendinosus and semimembranosus muscles. Muscle biopsy of one of the patients showed frequent eosinophilic sarcoplasmic inclusions and presence of few rimmed vacuoles. Ultrastructural study revealed sarcoplasmic accumulation of dense granulofilamentous material suggestive of myofibrillar myopathy. All the patients carried homozygous, very rare, damaging variants in the DNAJB4 gene: two stop gains (c.856A>T: p.Lys286* and c.74G>A: p.Arg25*) and a missense change (c.785T>C: p. Leu262Ser) predicted highly damaging by the in-silico tools. The variant segregated with the disease. Protein studies revealed absence of DNAJB4 protein in a patient muscle and fibroblasts compared to control.



Pedigrees of three families carrying homozygous, very rare, damaging variants in the DNAJB4 gene.



Muscle MRI of two probands showing a similar selective involvement of semitendinosus and semimembranosus muscles



MB of the proband AII:1 showed frequent eosinophilic sarcoplasmic inclusions and Ultrastructural study revealed sarcoplasmic accumulation of dense granulofilamentous material suggestive of myofibrillar myopathy.

Conclusion: We established recessive mutations in DNAJB4 as a possible cause of a novel form of neuromuscular disorder.

Disclosure: MYO-SEQ was funded by Sanofi Genzyme, Ultragenyx, LGMD2I Research Fund, Samantha J. Brazzo Foundation, LGMD2D Foundation and Kurt+Peter Foundation, Muscular Dystrophy UK, and Coalition to Cure Calpain 3.

Ageing and Dementia 1

OPR-040

Cortical remodeling across the lifespan in healthy brain reveals structural network vulnerability to neurodegeneration

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Background and aims: Aging is the main risk factor for most of the neurodegenerative diseases. The aim of this study was to investigate typical cortical thinning changes across lifespan in the healthy brain revealing structural network vulnerability to neurodegeneration.
Methods: The cohort included 128 healthy individuals aged 20–85 years that underwent an MRI scan. Structural T1-weighted images were used to estimate vertex-wise cortical thickness maps, then grouped into 83 regions.
For each region, cortical thickness trajectory with advancing age was estimated, including sex as covariate. Additionally, all regions were ranked based on their relative thickness at the end of the observed lifetime, assessing regional changes over time. Finally, regional mean thickness was correlated with relative change over time.
Results: The highest cortical thinning was observed in the temporal lobe (parahippocampal, entorhinal, superior and middle temporal and fusiform), in the frontal lobe (lateral orbitofrontal, superior and inferior frontal and rostral anterior cingulate), in the parietal lobe (the isthmus of cingulate, precuneus, supramarginal and inferior parietal) and in the insular cortex. Interestingly, occipital regions (cuneus, lateral occipital, lingual, pericalcarine), and motor and premotor areas (precentral, postcentral and paracentral regions) showed the least cortical thickness change relative to the whole brain. Finally, positive correlation was found between mean regional thickness and its relative change over time.
Conclusion: This study highlights structural vulnerability of brain regions to aging. Furthermore, results provide information concerning trajectories of normal brain aging, identifying those areas that might be more vulnerable to the attack of neurodegeneration.
Disclosure: Supported by: European Research Council (StG-2016_714388_NeuroTRACK).

OPR-041

Ocrelizumab treatment in patients with relapsing-remitting and progressive MS: a real-world experience

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Background and aims: We aim to provide first experience real-world effectiveness and safety data in relapsing-remitting (RR-), primary-progressive (PP-) and secondary-progressive multiple sclerosis (SP-MS) patients and to evaluate possible predictors of treatment response.
Methods: Demographic characteristics, effectiveness outcomes (Expanded Disability Status Scale (EDSS) progression, radiological activity data, NEDA-3 status), immunological parameters and adverse events (AEs) were recorded at baseline and throughout the follow-up (FU).
Results: 153 subjects were included in the analysis (93 RR-MS, 43 PP-MS, 17 SP-MS; 60% females); baseline mean(SD) age was 41.9(11.4) years, mean(SD) disease duration (DD) 10.3(9.9) years, mean(SD) annualized relapse rate (ARR) 0.5 (0.7), median(IQR) EDSS 3.5 (2–5.5). At two years-FU, percentage disability worsening-free patients were 90.5%, 64.7% and 68.8%, of MRI-activity-free patients 67.1%, 72.7% and 81.3% and of NEDA-3 patients 62.1%, 54.6% and 55.1% for RR-MS, PP-MS and SP-MS, respectively. Lower baseline EDSS, shorter DD, younger age, higher ARR and baseline MRI-activity were associated with reduced risk of disability worsening, while previous DMT exposure and baseline MRI-activity with increased risk of radiological activity. Treatment-naïve patients had higher probability of achieving NEDA-3. At six months-FU CD8+ cell count were higher in "early inflammatory" vs stable patients (464 vs 339; p=0.001). Upper respiratory tract infections were the most frequently observed AEs.
Conclusion: We showed that ocrelizumab is a good and globally safe treatment option in patients with RR-MS, PP-MS and SP-MS, especially if initiating treatment in the early phases of the disease and for treatment-naïve patients. Our data suggest that higher levels of CD8+ cells could be associated to early inflammatory activity.
Disclosure: The present study received no fundings

OPR-042

THE BRAIN CORRELATES OF BEHAVIORAL DISTURBANCES IN FRONTOTEMPORAL DEMENTIA

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Background and aims: Various studies have researched singular or clusters of behaviors in frontotemporal dementia (FTD) correlating them with regional brain atrophy in structural MRI data, or hypometabolism in FDG-PET images, but a multimodal approach is lacking. We identify the brain correlates of modes of variation (i.e., factors) explaining the variability of behavioral and psychological symptoms (BPSD) in frontotemporal dementia (FTD) using multimodal imaging.

Methods: Imaging and behavioral data from 93 FTD patients acquired at NIH were analyzed. They underwent extended neuropsychological assessment including several scales measuring BPSD (UCLA NPI, FrSBe, and Neurobehavioral rating scale), T1-weighted MRI, and FDG-PET imaging. Factor analysis was used on the behavioral data to identify modes of variation of BPSD potentially pointing to few common neurobiological substrates across the FTD sample. The identified modes were then related to intersubject brain variability using a newly developed fusion method run on maps of gray matter volume and FDG metabolism obtained.

Results: A factor related to decreased emotional/cognitive interaction (loading scores of apathy, executive dysfunction, withdrawal) correlated with volume and function of the right anterior cingulate and orbito-frontal cortex. A factor expressing variability on mutacism versus disinhibition/euphoria continuum was associated with dysfunction of the right superior primary motor cortex. A factor related to the presence of hallucinations/delusions/suspiciousness was associated with dysfunction of the right anterior insula.

Conclusion: BPSD variability in patients with FTD can be explained by three major modes of variations, each associated with intersubject brain structure/function variability of the right frontal lobe.

Disclosure: I have no actual or potential conflict of interest in relation to this program/presentation.

OPR-043

Sex influences the effect of cognitive reserve on Subjective Cognitive Decline

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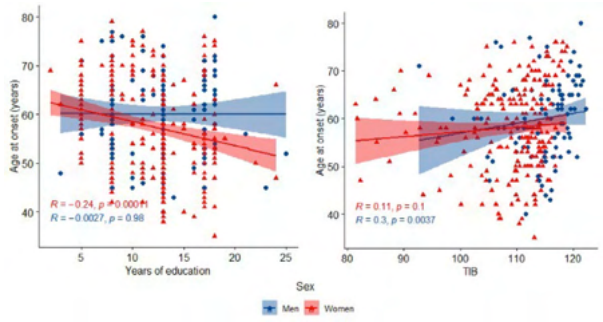
Background and aims: Subjective Cognitive Decline (SCD) is as a self-experienced decline in cognitive capacity with normal performance on standardized cognitive tests and has been shown to increase risk of Alzheimer's disease. The aim of our study was to evaluate factors influencing age at onset and severity of SCD.

Methods: We included 382 SCD patients, who underwent clinical evaluation, neuropsychological assessment, evaluation of premorbid intelligence by the Test di Intelligenza Breve (TIB), cognitive complaints by the Memory Assessment Clinics-Questionnaire (MAC-Q), and depressive symptoms by Hamilton Depression Rating Scale (HDRS), and Apolipoprotein E (ApoE) genotyping.

Results: Proportion between women and men was significantly different (68.6%, 95% C.I. 65.0–73.3 vs 31.4%, 95% C.I. 29.0–34.4). Women were younger than men at onset of SCD and at the baseline visit (p=0.02), had lower years of education (p=0.007), lower TIB scores (p<0.001), and higher HDRS (6.3±4.1 vs 5.12±3.8, p=0.007) and MAC-Q scores (26.3±3.1 vs 25.0±2.7, p=0.012) (Fig1). TIB was directly associated with age at onset of SCD both in women and in men, while years of education was inversely associated with age at onset only in women (Fig.2). On the whole sample, sex was the only factor influencing MAC-Q. When we ranked patients according to sex, TIB was directly associated with MAC-Q only in men.

	Women n = 262	Men n = 120	p
Age at baseline in years	61.7 (±9.0)	64.1 (± 8.4)	**0.020**
Age at onset in years	57.8 (± 9.5)	60.9 (± 8.4)	**0.026**
Disease duration in years	3.9 (± 3.6)	3.4 (± 3.4)	0.726
Family history of AD	50.8 %	48.4 %	0.738
Years of education	11.5 (± 4.6)	12.90 (± 4.2)	**0.007**
TIB	109.0 (± 7.4)	114.8 (± 5.4)	**<0.001**
MMSE	27.9 (± 2.0)	28.4 (± 1.9)	**0.039**
HDRS	6.3 (± 4.1)	5.12 (± 3.8)	**0.007**
MAC-Q	26.3 (± 3.1)	25.0 (± 2.7)	**0.012**
APOE ε4+	22.2 %	41.7 %	**0.013**

Comparison of baseline features between women and men in SCD.



Correlation between premorbid intelligence and years of education with age at onset of SCD in women and men.

Conclusion: While premorbid intelligence was associated with both age at onset and severity of cognitive complaints in men, premorbid intelligence and years of education had opposite effect on age at onset of SCD in women. Sex might modulate the effect of cognitive reserve on SCD.
Disclosure: Nothing to disclose.

OPR-044

In-depth phenotypic description of TBK1 mutations; a frequent cause of FTD and ALS in the Flanders-Belgian population

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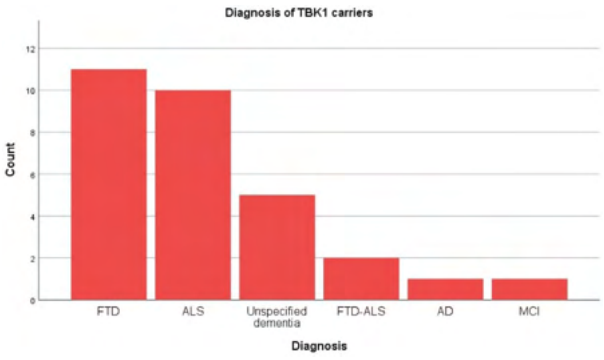
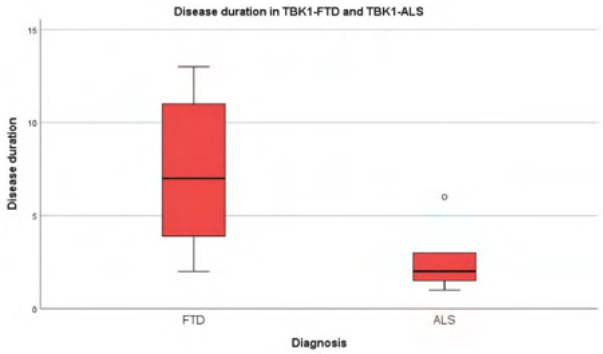
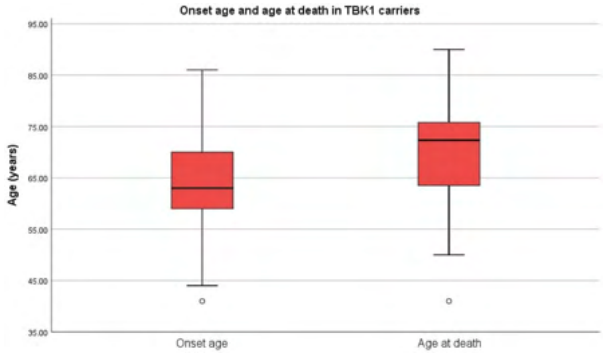
Background and aims: Pathogenic LOF and missense mutations in the TBK1 gene are associated with frontotemporal lobar degeneration (FTLD) and amyotrophic lateral sclerosis (ALS). We report the prevalence and phenotype of TBK1 mutation carriers in the Flanders-Belgian population.
Methods: Screening Flanders-Belgian FTD (n=678), ALS (n=220) and FTD-ALS (n=46) patient cohorts for mutations in TBK1 revealed 19 carriers of pathogenic mutations. We sampled and screened family members, totalling a carrier cohort of 47 individuals. We collected clinical and neuropathological data.
Results: Overall, frequency of TBK1 mutations was 2.0%, with 1.3% in FTD, 3.6% in ALS and 4.3% in FTD-ALS. Among 47 carriers, 30 were affected: FTD (n=11, 36.7%), ALS (n=10, 33.3%), unspecified dementia (n=5, 16.7%), FTD-ALS (n=2, 6.7%), mild cognitive impairment (n=1, 3.3%) and Alzheimer's disease (n=1, 3.3%). In the FTD group, behavioral variant FTD (bvFTD) was the most common phenotype (81.8%) but primary progressive aphasia also occurred (18.2%). Mean onset age and disease duration were 63.0 and 6.4 years (ranges 41–86 and 0–24 years). ALS patients had a significantly shorter disease duration averaging 2.6 years (range 0–6). Neuropathology confirmed FTLD-TDP type B.



Clinical diagnoses of TBK1 mutation carriers



Disease duration in patients with TBK1-FTD compared with TBK1-ALS. A significantly shorter disease duration was seen in the latter.



Representation of the range of onset ages and ages at death in symptomatic TBK1 mutation carriers

Conclusion: Pathogenic mutations in TBK1 are a frequent cause of FTD, ALS and particularly of FTD plus ALS in the Flanders-Belgian population. The most common phenotypes were FTD (81.8% bvFTD, 18.2% PPA), ALS and unspecified dementia. Disease duration significantly correlated with clinical phenotype. Neuropathology showed FTLD-TDP type B.

Disclosure: Nothing to disclose.

OPR-045

Extensive genetic and phenotypic description of MAPT p.R406W in the Flanders-Belgian population

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Background and aims: The missense mutation p.R406W in the MAPT gene is associated with frontotemporal lobar degeneration (FTLD) pathology and an atypical, Alzheimer's disease (AD)-like phenotype. In our Flanders-Belgian patient cohort, we identified 10 p.R406W carriers. Of three index carriers, we sampled family members, generating a total cohort of 55 p.R406W carriers. We analysed phenotypical and genetic characteristics.

Methods: Longitudinal follow-up over 19 years provided clinical and neuropathologic data. We investigated potential modifying effects of MAPT H1/H2 and APOE genotypes.

Results: Of 55 p.R406W carriers, 39 were symptomatic. Allele-based haplotype sharing analysis confirmed a genetic kinship among all carriers suggesting a common ancestor. Frequent diagnoses were dementia (unspecified) (43.6%), AD (28.2%) and behavioral variant FTD (bvFTD) (25.6%). Average onset age and disease duration were 59.8 and 12.7 years (ranges 40–75, 5–25). Age at death differed significantly between clinical subgroups (69.3 in bvFTD, 78.3 in AD). Common symptoms among carriers were disinhibition and behavioural problems in all groups (72.7%). CSF biomarker profiles showed decreased A1-42 and A1-42/A1-40 ratio, and elevated P-tau and T-tau. Neuropathology is FTLD-tau. We observed a shorter disease duration in carriers of an APOE 4 allele compared to non-carriers.

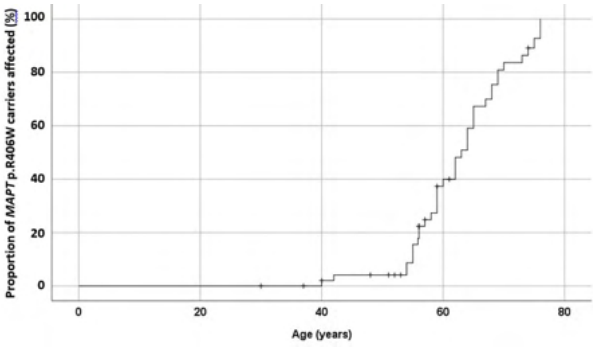

Figure 1. Risk liability curve for MAPT p.R406W mutation carriers.

Risk liability curve for MAPT p.R406W mutation carriers

	Neuroimaging		CSF biomarkers			
Diagnosis	Primarily HC/TP/T involvement	Primarily FT involvement	Decreased $A\beta_{1-42}$	Decreased $A\beta_{1-42}$/ $A\beta_{1-40}$	Elevated T-tau	Elevated P-tau
bvFTD (n = 7)	42.9% (n = 3)	28.6% (n = 2)	100% (n = 1)	NA	0% (n = 1)	0% (n = 1)
AD (n = 7)	57.1% (n = 4)	14.3% (n = 1)	100% (n = 4)	75% (n = 4)	50% (n = 4)	50% (n = 4)
D (n = 1)	0%	0%	NA	NA	NA	NA
MCI (n = 1)	0%	0%	NA	NA	NA	NA

Table 7. Trends in results of neuroimaging and CSF biomarkers in *MAPT* p.R406W mutation carriers with sufficient clinical data. Alzheimer's disease (AD), behavioral variant frontotemporal dementia (bvFTD), mild cognitive impairment (MCI), temporal (T), frontotemporal (FT), temporoparietal (TP), hippocampal (HC), amyloid β_{1-42} ($A\beta_{1-42}$), amyloid β_{1-40} ($A\beta_{1-40}$), total tau (T-tau), hyperphosporylated tau (P-tau).

Results of neuroimaging and CSF biomarkers in mutation carriers. Alzheimer's disease (AD), behavioral variant frontotemporal dementia (bvFTD), mild cognitive impairment (MCI), temporal (T), frontotemporal (FT), temporoparietal (TP), hippocampal (HC), amyl

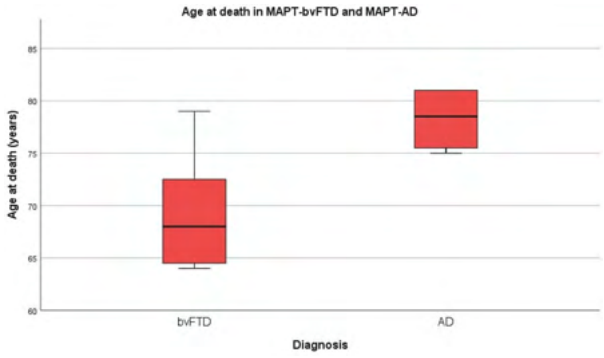

Figure 2. Age at death in p.R406W MAPT mutation carriers with a clinical phenotype of bvFTD compared to clinical AD. A significantly earlier death was found in bvFTD.

Conclusion: We observed a nonconforming clinical phenotype of p.R406W carriers in the Flemish-Belgian cohort with 25.6% bvFTD. Contrary to previous reports, prominent behavioural symptoms were highly frequent in the entire cohort (72.7%). Ages at onset and death varied widely but, intriguingly, correlated with clinical diagnosis, lower in bvFTD than AD phenotypes. CSF biomarkers showed some AD-like abnormalities.
Disclosure: Nothing to disclose.

OPR-046

Accuracy of 18F-FDG PET at the individual level in MCI-LB versus MCI-AD

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Background and aims: 18F-FDG PET is an established supportive biomarker in dementia with Lewy bodies (DLB) but its diagnosis accuracy is still uninvestigated in prodromal DLB (MCI-LB) in which the typical DLB metabolic pattern may be difficultly recognized at the individual level. Semiquantitative analysis is thought to enhance accuracy especially in moderately-skilled readers, but its incremental value with respect to visual assessment in this peculiar DLB stage is still unknown.
Methods: We assessed the diagnostic accuracy of visual assessment of 18F-FDG PET by six expert readers, blind to diagnosis, in discriminating two matched groups of patients (40 with prodromal AD, MCI-AD, and 39 with MCI-LB), both confirmed by in vivo biomarkers of either amyloidosis or dopamine transporter (DAT)-SPECT impairment, respectively. After two months, the readers were asked to re-evaluate the scans having for each patient also the T-maps obtained by the single-subject semiquantitative analysis (SPM-12) with respect to a control group of 40 age- and sex-matched healthy subjects.
Results: Mean diagnostic accuracy of visual assessment was 76.8±5.0% (range 68.4–83.5%) and did not significantly benefit from adding the semiquantitative analysis (77.4±8.3%, range 63.3–87.3%), regardless of the readers' years of expertise. Inter-rater reliability was good in both conditions (ICC 0.81[0.74–0.87] and 0.83[0.76–0.88], respectively).
Conclusion: We found a moderate diagnostic accuracy of 18-FDG PET in distinguishing between MCI-AD and MCI-LB patients which seems valuable considering the limited accuracy of DAT-SPECT in prodromal DLB. We also provided evidence of the poor utility of adding semiquantitative tools to visual assessment, both in moderately and highly expert readers
Disclosure: Nothing to disclose.

Cognitive Neurology/Neuropsychology

OPR-047

Remote white matter integrity improves prediction of cognitive outcome after ischemic stroke

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Background and aims: Cognitive impairment after ischemic stroke is frequent, especially after middle cerebral artery occlusion. Beyond clinical measures, advanced imaging modalities such as diffusion tensor imaging (DTI) and resting-state functional connectivity (rsFC) have been shown to improve prediction of post-stroke motor outcome over and above conventional imaging parameters. However, comparable studies on cognitive outcome are scarce.
Methods: We investigated patients with MRI-confirmed middle cerebral artery infarction and healthy controls. Cognitive outcome was determined using the Symbol Digit Modalities Test (SDMT), measuring processing speed. Associations between acute fractional anisotropy (FA) and rsFC with cognitive outcome were examined, and regression analyses were performed to predict post-stroke cognitive outcome further considering demographics (age, education), clinical measures (NIHSS at baseline), as well as extent and location of infarction and white matter hyperintensities (WMH).
Results: 36 patients (mean age=64.7 years, 33.3% female, median admission NIHSS=9.0) were investigated at the acute stage and three months post-stroke. 15 healthy controls (mean age=57.3 years, 53.3% female) were also assessed at two time-points. Patients showed decreased FA and rsFC three months post-stroke compared to healthy controls. Also, acute FA and rsFC correlated with processing speed three months post-stroke in patients. FA of corpus callosum body, splenium and forceps major at the acute stage predicted processing speed three months post-stroke independently from demographics, NIHSS at baseline, stroke location and volume and WMH, explaining 28% of additional variance (overall variance 56%).
Conclusion: Remote white matter integrity at the acute stage improves prediction of cognitive outcome beyond clinical measures, stroke location and volume.
Disclosure: Nothing to disclose.

OPR-048

Altered resting state dynamic functional connectivity of the precuneus contributes to cognition and depression in NMOSD

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Background and aims: In neuromyelitis optica spectrum disorders (NMOSD), cognitive impairment (CI) is frequent, but its substrates are unclear. Functional MRI (fMRI) studies disclosed an association between CI and damage of the precuneus (PCUN) in several neurological conditions. Dynamic changes of resting-state (RS) functional connectivity (FC) might contribute to brain functional reorganization.
Methods: In this 3.0 T RS fMRI study, 27 aquaporin-4 (AQP4)-positive NMOSD patients and 30 age- and sex-matched healthy controls (HC) underwent a neuropsychological evaluation including Rao's battery and Beck Depression Inventory II scores. A cognitive impairment index (CII) was derived. Dynamic FC (DFC) of bilateral PCUN was assessed by means of sliding-window seed-voxel correlation analysis and its standard deviation across windows used as a measure of dynamicity (the higher the better). Age- and sex-adjusted between-group dFC comparisons and correlations with cognitive scores were assessed using full-factorial models.
Results: Compared to HC, patients had reduced PCUN-dFC with rectus/olfactory bulb, post-central gyrus, superior temporal gyrus, inferior occipital/fusiform gyri and the caudate nucleus. Conversely, increased dFC within the PCUN and between PCUN and middle temporal gyrus, thalamus, insula, putamen, and cerebellar crus-1 was observed. 63% of patients had depressive symptoms, whose burden correlated with intra-PCUN-dFC and with PCUN-dFC with insula and cerebellar crus-1. 48t% of patients had CI and global CII correlated with intra-PCUN-dFC and with PCUN-dFC with the insula and the middle temporal gyrus.
Conclusion: In NMOSD, PCUN-dFC abnormalities contribute to neuropsychological performance. Higher dynamic connections with the temporal lobe and limbic/cerebellar regions were detrimental for cognition and depression, respectively.
Disclosure: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

OPR-049

RISCOP – Cognitive Profile in a Portuguese cohort of Radiological Isolated Syndrome patients: a case-control study

V. Carvalho [1], C. Soares [1], I. Gomes [2], A. Carvalho [3], F. Serrazina [1], A. Rodrigues [4], J. Pinheiro [3], I. Bras Marques [4], F. Correia [5], A. Correia [4], J. Correia Sa [4], L. Suosa [2], J. Vale [6], M. Sá [1], C. Sousa [7], J. Ferreira [4]
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Background and aims: Radiologically isolated syndrome (RIS) refers to the incidental discovery of white matter lesions suggestive of MS, on brain MRI, in asymptomatic patients. Recent studies suggest similar features of cognitive impairment between RIS and MS patients. Also, lower levels of health-related quality of life (QOL) and fatigue are reported. We aimed to characterize the cognitive profile of a multicentric Portuguese cohort of RIS patients and compare with a control group.
Methods: Multicentric comparative study of a cohort of RIS adult patients, with age and gender-matched controls. We conducted participants interviews, collected clinical data and applied the BICAMS battery and self-reported questionnaires (HADS, MFIS, MSQOL-54).
Results: 61 RIS patients (median age 46 years, IQR [33–52], 72% women) and 19 controls (median age 32 years, IQR [28–48], 71% women) were included. Prevalence of cognitive impairment did not differ between groups (16% RIS Vs. 10% controls, p=0.579). We found no differences on the BICAMS tests between groups, although the California Verbal Learning Test (CVLT-II) score results trended to significance, with a lower value on the RIS group (53.9 vs. 59.3, p=0.066). There were no significant differences regarding fatigue, QOL, anxiety/depression scores.
Conclusion: This is the first Portuguese study assessing cognitive profile with BICAMS on a cohort of RIS patients. A non-neglectable part of our cohort presented cognitive impairment. Our findings suggest that a more pronounced impairment of verbal memory and learning, evaluated by CVLT-II, might be present in RIS patients compared to controls. BICAMS should be assessed on future studies with larger cohorts.
Disclosure: Nothing to disclose.

OPR-050

NODDI microstructural abnormalities in normal-appearing gray and white matter contribute to cognitive impairment in MS

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Background and aims: Heterogeneous processes contribute to cognitive impairment in multiple sclerosis (MS). Using neurite orientation dispersion and density imaging (NODDI), we explored the associations between microarchitecture abnormalities of focal lesions and normal-appearing (NA) tissues and cognitive impairment in patients with MS (PwMS).
Methods: 152 PwMS and 48 healthy controls (HC) underwent a brain 3T acquisition. PwMS with one abnormal test in two domains were defined as cognitively impaired (CI). A cognitive impairment index (CII) was also derived. Using NODDI, intracellular (ICV_f) and extracellular volume fractions (ECV_f) and orientation dispersion index (ODI) were assessed in cortical and white matter (WM) lesions, thalamus, NA-cortex and NAWM.
Results: 52 (34.2%) PwMS were CI. Compared to HC, both CI and cognitively preserved (CP) PwMS showed significantly decreased NA-cortex, thalamic and NAWM ICV_f ($p<0.001$) and NA-cortex ODI ($p=0.003$), and increased NAWM ECV_f ($p<0.001$). CI PwMS showed also a significantly decreased thalamic ODI ($p=0.018$) and increased NAWM ODI ($p=0.005$). CI vs CP PwMS had significantly decreased NA-cortex, thalamic and NAWM ICV_f ($p=0.016$) and thalamic ECV_f ($p=0.009$), and increased NAWM ECV_f and ODI ($p=0.001$). No cortical and WM lesion microstructural differences were found in CI vs CP PwMS. NA-cortex ICV_f and NAWM ICV_f and ODI were significantly correlated with CII (r from -0.24 to 0.30 p from 0.006 to 0.047).
Conclusion: NA-cortex, thalamic and NAWM neuro-axonal loss, together with NAWM inflammation, gliosis and loss of tissue coherence, are associated with cognitive impairment in MS. NODDI could disentangle in vivo the complex processes determining cognitive dysfunctions.
Disclosure: This study was supported by Fondazione Italiana Sclerosi Multipla with a senior research fellowship (FISM2019/BS/009) and a research grant from (FISM2018/R/16), and financed or co-financed with the '5 per mille' public funding.

OPR-051

Consciousness in Neurocritical Care Cohort Study Using fMRI and EEG (CONNECT-ME)

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Background and aims: Patients with acute brain injury who appear clinically unresponsive may show signs of covert consciousness when examined by functional MRI (fMRI) or electroencephalography (EEG). The main objective of this ongoing multimodal study is to facilitate individualized assessment of unresponsive patients with disorders of consciousness (DOC) in the ICU for signs of preserved consciousness.

Methods: We assess acute brain-injured ICU patients for preserved consciousness by clinical and multimodal evaluation using active, passive and resting state fMRI and EEG paradigms (Figure 1). EEG and fMRI data are correlated to clinical consciousness level at time of inclusion, discharge and long-term follow-up. EEG data is analyzed visually by two board-certified neurophysiologists and with automated EEG measures, previously validated on patients with chronic DOC. Automated EEG measures are utilized to calculate the probability of being in a consciousness level above unresponsive wakefulness state (P-MCS).

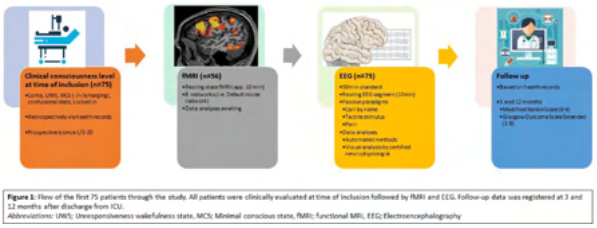

Figure 1

Results: As of Dec. 2020, 102 patients have been included. The following results are from the first 75 patients (Table 1 and Figure 2). No significant correlation was found between P-MCS>50% and clinical consciousness level at time of inclusion, discharge and 3-month follow-up. We found significant correlation (p-value<0.05) between P-MCS >50% and long-term favorable follow-up outcome at 12 months. fMRI and visual EEG data analysis are ongoing.

Table 1: Characteristics of study population

Characteristics	All patients (N = 75)	≥MCS (N = 30)	≤UWS, (N = 45)	p- value
Age – Yr				
Mean (SD)	50.1 (19.2)	46.6 (16.7)	52.4 (20.6)	0.2031
Gender – no. (%)				
Male	43 (57.3)	15 (50)	28 (62.2)	0.6112
mRS prior to admission – no. (%)				
0-2	67 (89.3)	27 (90.0)	30 (88.9)	1.000
>2	8 (10.7)	3 (10.0)	5 (11.1)	-
Comorbidity prior to admission (any), no. (%) [a]	**54 (73.3)**	**20 (66.7)**	**34 (75.6)**	0.440
Cardiopulmonary	30 (40.0)	9 (30.0)	20 (46.7)	0,235
Diabetes	9 (12.0)	3 (10.0)	6 (20.0)	0,733
Neurology, cerebrovascular	9 (12.0)	4 (13.3)	5 (16.7)	1.000
Neurology, Epilepsy	6 (8.0)	4 (13.3)	2 (4.4)	0,210
Neurology, other	16 (21.3)	7 (23.3)	9 (20.0)	0.779
Psychiatry, any	12 (16.0)	6 (20.0)	6 (13.3)	0.526
Other comorbidities	33 (44.0)	11 (36.7)	21 (48.9)	0.477
Cause of ICU admission, no. (%)				
Traumatic brain injury	22 (29.3)	7 (23.3)	15 (33.3)	0,441
Ischemic stroke	11 (14.7)	4 (13.3)	7 (15.6)	1.000
Subarachnoid or intracerebral hemorrhage	8 (10.7)	6 (20.0)	2 (4.4)	0,053*
Cardiac arrest	10 (13.3)	0 (0)	10 (22.2)	0,005*
Other causes	24 (32.0)	13 (43.3)	11 (24.4)	0,129
Cerebral scan findings during admission, no. (%)				
Normal	7 (0.9)	4 (13.3)	3 (6.7)	0,210
Focal or mild bilateral lesions	12 (1.6)	6 (20.0)	6 (13.3)	0,526
Diffuse severe bilateral, DAI or brainstem lesion	48 (64.0)	20 (66.7)	28 (62.2)	0,808
Anoxic brain damage	9 (12.0)	0 (0)	9 (20.0)	0,009*
GCS score at ICU admission, no. (%)				
Median (Min - Max)	6 (3 – 14)	9 (4 – 14)	5 (3 – 9)	<<0,001**
FOUR score at ICU admission, no. (%)				
Median (Min – Max)	8 (0 – 16)	11 (5 – 16)	6 (0 – 10)	<<0,001**
Time from ICU admission to index EEG, days				
Mean (SD)	15.9 (29.4)	18.17 (11.4)	14.4 (14.3)	0,209
Duration of ICU admission, days				
Mean (SD)	31.9 (24.8)	36.1 (29.4)	29.1 (21.0)	0.2339
Death during ICU admission – no. (%)	**28 (37.3)**	**2 (6.7)**	**26 (57.8)**	<<0.001 **
WLST due to poor prognosis	26 (34.7)	1 (3.3)	25 (55.6)	0,140[b]
Other causes (sudden clinical deterioration)	2 (2.7)	1 (3.3)	1 (2.2)	-

[a] Percentage of comorbidities do not add up to 100 as patients could have multiple comorbidities.
[b] no.total in this calculation is total number of deaths (28) and not the full population of 75.
*Indicates p-value < 0,05
**Indicates p-value < 0,001
Abbreviations: SD; Standard Deviation, mRS; Modified Rankin Scale, ICU; Intensive Care Unit, DAI; Diffus Axonal Injury, GCS; Glasgow Coma Scale, FOUR; Full Outline of UnResposivness, WLST: Withdrawal of Life-Sustaining Therapy

Table 1

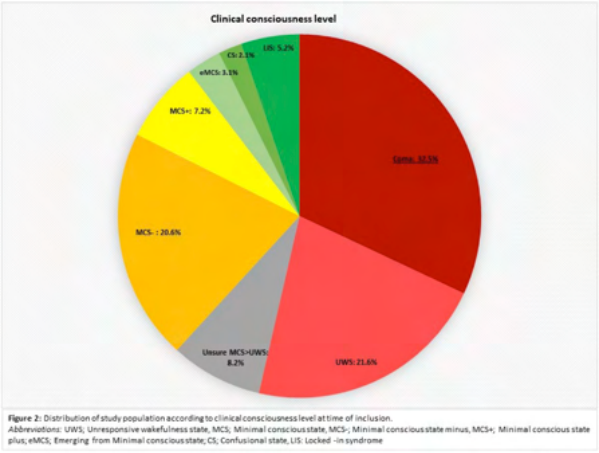

Figure 2: Distribution of study population according to clinical consciousness level at time of inclusion.
Abbreviations: UWS; Unresponsive wakefulness state, MCS; Minimal conscious state, MCS-; Minimal conscious state minus, MCS+; Minimal conscious state plus; eMCS; Emerging from Minimal conscious state; CS; Confusional state, LIS: Locked -in syndrome

Figure 2

Conclusion: In acute brain-injured patients with DOC previously thought of as unconscious, a multimodal approach, including automated EEG measures, may help detect covert consciousness, thereby contributing personalized prognostication.

Disclosure: Nothing to disclose.

OPR-052

Unravelling the neural basis of spatial delusions after stroke

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Background and aims: Knowing explicitly where we are is an interpretation of our spatial representations. Spatial delusions are disrupting syndromes in which patients present a resilient belief of spatial mislocation. Here, we studied the largest sample of patients with spatial delusions after stroke to shed light on their neurobiology.
Methods: In a prospective, cumulative, case-control study, we screened 400 patients with acute right hemispheric stroke. We included 64 cases presenting spatial delusions and 233 controls. first, lesions were delimited and normalized. Then, we computed structural and functional disconnection maps using methods of lesion-track and network-mapping. The maps were compared, controlling for nuisance variables. 2nd, we built a multivariate logistic model including clinical, behavioural and neuroimaging data. Finally, we performed a nested cross-validation of the model with a support-vector machine analysis.
Results: We found a structural disconnection map that was significantly associated with spatial delusions. It was the strongest predictor of the syndrome and included two distinct streams, connecting right fronto-thalamic and right occipito-temporal structures. Significant functional disconnection was observed in the right precuneus, and a functional-structural link was demonstrated. In the multivariate model, the independent predictors of spatial delusions were the structural disconnection map, lesion sparing of right dorsal fronto-parietal regions, age and anosognosia. Good discrimination accuracy was demonstrated (median area under the curve=0.80, interquartile range 0.75–0.85).
Conclusion: Our results revealed the circuits associated with the abnormal spatial-emotional binding and the defective updating of spatial representations underlying spatial delusions. This novel data may contribute to better understand the pathophysiology of delusional syndromes after stroke.
Disclosure: Nothing to report.

COVID-19

OPR-053

Multiparametric analysis reveal no intrathecal inflammation in COVID-19 associated neurological syndromes

R. Bernard-Valnet [1], S. Perriot [2], M. Canales [1], B. Pizzarotti [1], L. Caranzano [1], M. Castro-Jimenez [1], J. Epiney [3], S. Vijiala [1], P. Salvioni Chiabotti [1], A. Anichini [4], A. Salerno [1], M. Perreau [5], G. Pantaleo [5], G. Greub [6], R. Du Pasquier [4]

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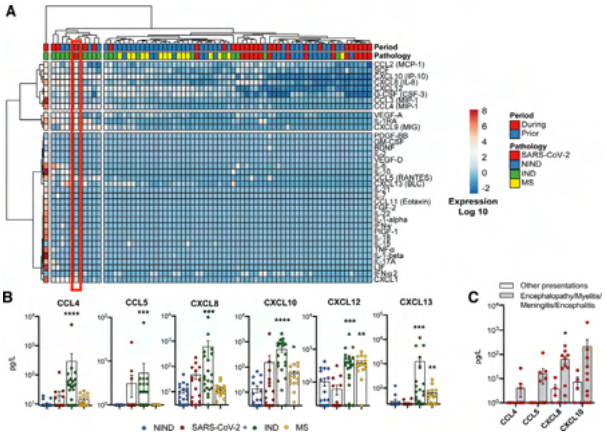
Background and aims: Coronavirus disease (COVID-19) has been associated with a large variety of neurological disorders. However the mechanisms underlying these neurological complications remain elusive. In this study we aimed at determining whether neurological symptoms were caused by SARS-CoV-2 direct infection of by pro-inflammatory mediators.

Methods: We checked for SARS-CoV-2 RNA by RT-qPCR, SARS-CoV-2-specific antibodies and for 48 cytokines/chemokines/growth factors (by Luminex) in the cerebrospinal fluids (CSF) ± sera of a cohort of 17 COVID-19 patients with neurological presentation and 55 neurological control patients (inflammatory [IND], non inflammatory [NIND], multiple sclerosis [MS]).

Results: We found SARS-CoV-2 RNA and antibodies specific for this virus in the CSF of 0/17 and 8/16 COVID-19 patients, respectively. The presence of SARS-CoV-2 antibodies was explained by a rupture of the blood brain barrier (passive transfer) in 6/16 (38%). An intrathecal synthesis of SARS-CoV2-specific antibodies was present in 2/16 patients. Of the four categories of tested patients, the CSF of IND exhibited the highest level of chemokines (CCL4, CCL5, CXCL8, CXCL10, CXCL12, and CXCL13), followed by the CSF of MS patients (CXCL12, and CXCL13). There was no significant difference between COVID-19 and NIND patients, even if some chemokines (CCL4, CCL5, CXCL8, andCXCL10) tended to be higher in the former. Interestingly, among COVD-19 patients, the CSF of those with a severe disease (encephalitis/encephalopathy) contained higher levels CXCL8 and CXCL10 than those with other neurological presentations.



Cytokines/Chemokines/Growth factor in the CSF of patients with neurological presentation of SARS-CoV-2

Conclusion: Our results do not show obvious SARS-CoV-2 infection of the central nervous system, but point to a mild inflammatory reaction reflecting an astrocytic reaction.

Disclosure: Nothing to disclose.

OPR-054

Brainstem damage in COVID-19

G. Bulfamante [1], L. Campiglio [2], S. Coppola [1], M. Falleni [1], D. Chiumello [1], A. Priori [1], T. Bocci [1]
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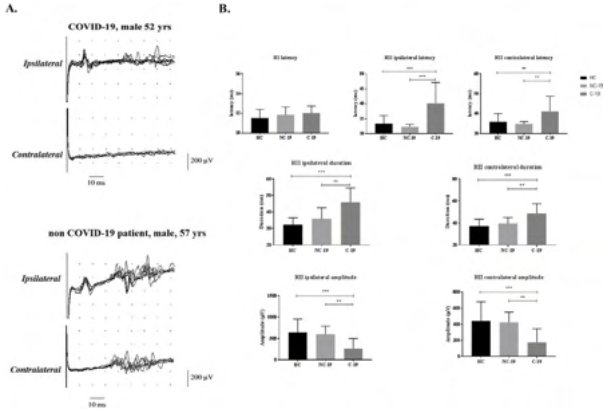
Background and aims: It has recently been proposed that SARS-CoV-2 might spread through the nervous system in a prion-like way, reaching respiratory centers in the brainstem. Here, we evaluated neuropathologically, neurophysiologically and clinically the brainstem involvement in COVID-19.

Methods: Neuropathological data were acquired from patients died for COVID-19 and COVID-19 negative; neuronal damage and the number of corpora amylacea (CA)/mm^2 were assessed. The expression of the "nuclear protein" of SARS-Cov-2 was also evaluated. To clarify whether neuropathological findings had a functional correlate, we studied the blink reflex (BR) in 11 COVID-19 patients, admitted to our Intensive Care Unit (ICU), and compared data both with healthy subjects and non COVID-19 ICU patients. An extensive neurological examination, comprising the corneal and glabellar reflexes, was also performed.

Results: Autopsies showed a high percentage of neuronal damage and a higher number of CA in the medulla oblongata of COVID-19 patients; immunohistochemistry revealed the presence of SARS-Cov-2 virus in the brainstem. Neurophysiologically, the RII component of the BR was selectively impaired in COVID-19 and, clinically, the glabellar reflex reduced or absent.



Neurophysiological findings. Note that the medullary RII response of the supraorbital blink reflex (BR) is impaired in COVID patients, compared both to controls and non-COVID ICU patients

Conclusion: Our findings provide the first combined neuropathological, neurophysiological and clinical evidence of SARS-Cov-2-related brainstem involvement, especially at the medullary level, suggesting a neurogenic component of respiratory failure.

Disclosure: The Authors have no conflicts to declare.

OPR-055

Neurological manifestations after COVID-19 illness: Observations in one of the largest COVID-19 centers in México.

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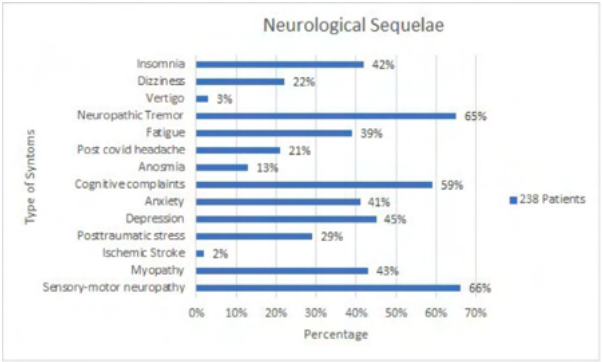
Background and aims: Since the beginning of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic in 2019, that causes human coronavirus disease 2019 (COVID-19), persistent symptoms among COVID-19 survivors have been described. Our objective is to report neurological sequelae in hospitalized COVID-19 survivors.

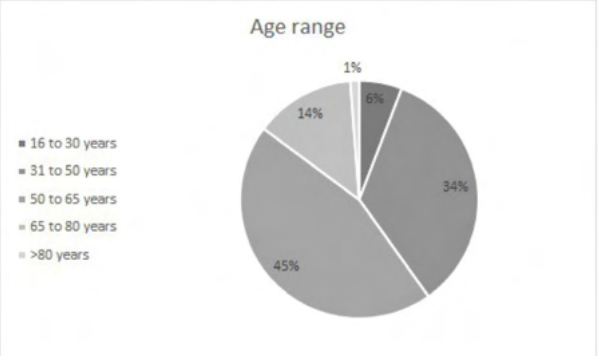
Methods: Our study included the neurological sequalae observed in 238 patients that were admitted at a single medical center with acute respiratory distress syndrome (ARDS) due to COVID-19. Three months after their hospital discharge, a complete neurological examination and a cognitive screening Montreal Cognitive Assessment (MoCA) test was applied by two neurologists in Mexico City, from August 31, 2020, to January 8, 2021.

Results: All patients were positive for SARS-CoV-2, tested via reverse-transcriptase-polymerase-chain-reaction (RT-PCR) assays of nasopharyngeal samples. The mean age of the cohort was 51 years. 97 patients (68.3%) needed mechanical ventilatory support. 52% patients exhibited a periphery oxygen saturation of less than 70% at admission. 10.6% were health care workers and eight patients had previous neurological disorders. The main neurological sequels found were sensory-motor neuropathy (66.4%), myopathic pain (43.9%), and cognitive complaints (59.7%) with an average MoCA score of 25.5 (46.6%). Furthermore, five patients were diagnosed with ischemic cerebral vascular disease, five patients presented seizures, 108 (45.6%) exhibited affective symptoms, and 52.2% patient reported a modified Rankin Scale score of less than 2.



Main neurological sequelae found in the 238 patients three months after their hospitalization.

Main comorbidities found in the 238 patients three months after their hospital discharge.



Age range of the 238 patients evaluated

Conclusion: The under-recognition of neurological sequelae may lead to an increase in the burden of COVID-19. Therefore having a multidisciplinary long-term follow-up is advisable in order to optimize treatment and to improve prognosis.
Disclosure: Nothing to disclose.

OPR-056

Neurological implications of COVID-19 – results of the LEOSS registry

N. Kleineberg [1], S. Knauss [2], E. Gülke [3], H. Pinnschmidt [3], C. Jakob [1], J. Vehreschild [1], P. Lingor [4], K. Hellwig [5], A. Berthele [4], G. Höglinger [6], G. Fink [7], M. Endres [8], C. Gerloff [9], C. Klein [10], J. Erber [4], C. Franke [11], C. Warnke [12]
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Background and aims: Register studies and cohort analyses of clinical data are essential to study neurological manifestations of COVID-19 at a large scale.
Methods: We analyzed neurological manifestations in COVID-19 patients, diagnosed before Aug 25th 2020, and registered in the European multinational LEOSS registry.
Results: Of the 3127 COVID-19 patients, 95.2% were hospitalized. In 54.4% at least one neurological symptom, and in 3.3% a new neurological complication occurred. Pre-existing neurological comorbidities were reported in 18.1% of the patients. Neurological symptoms were excessive tiredness (27.6%), headache (15.3%), nausea/emesis (14.0%), muscular weakness (13.2%), smell (6.9%), taste disorder (8.3%) and delirium (6.3%). Intracerebral bleeding occurred in 1.2%, ischemic stroke in 0.5%, and meningitis/encephalitis in 0.4%. Overall, the death rate was 17.5%. It was higher in patients with the following neurological comorbidities: dementia 38.0%, movement disorders 32.8%, and prior cerebrovascular disease 32.3%. A multivariable logistic regression model found age (OR 1.53), cardiovascular diseases (OR 1.74), muscle weakness (OR 1.40), pulmonary diseases (1.49) and male gender (OR 1.52) to be associated with a significantly increased risk for a critical COVID-19 disease course, failed recovery, and death.
Conclusion: The neurological manifestations revealed in COVID-19 patients of this study are mostly in agreement with previously published data. Several neurological conditions, such as prior cerebrovascular diseases or dementia appeared to be associated with a higher risk in unadjusted analyses, which was not confirmed in a multivariable analysis adjusting for confounding variables such as age and sex. These findings contrast previously published studies and stress the importance of considering putative confounds in medical statistics carefully.
Disclosure: Nothing to disclose.

OPR-057

COVID-19 and Guillain-Barré syndrome in early pandemia in Lombardia: increased incidence or increased seroprevalence?

F. Martinelli Boneschi [1], A. Salmaggi [2], M. Sessa [3], S. Canella [4], R. Xhani [4], E. Magni [5], M. Versino [6], C. Ferrarese [7], D. Zarcone [8], A. Albanese [9], G. Micieli [10], C. Zanferrari [11], A. Cagnana [12], C. Ferrante [13], L. Peverelli [14], A. Zilioli [2], D. Locatelli [15], M. Calloni [16], A. Colombo [16], C. Foresti [3], B. Frigeni [3], E. D'Adda [12], A. Rigamonti [2]

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Background and aims: Several studies reported increased incidence of Guillain-Barre' Syndrome (GBS) after Zika epidemic, SARS-CoV and MERS, and more recently SARS-CoV-2 infection. We estimate incidence and describe clinical characteristics and outcome of GBS in COVID-19 patients in one of the most affected regions by COVID-19 of the world, Lombardia.

Methods: A multi-center observational study on neurological complications in COVID-19 patients was conducted in 20 Neurology Units by the Italian society of Hospital Neuroscience (SNO). Adult patients admitted to Neurological units between February-April 2020 with COVID19-GBS were included.

Results: 38 COVID19-GBS patients had mean age of 60.7 years and male frequency of 86.8%. Mean interval between COVID-19 onset and GBS onset was 15.1 days. CSF albuminocytologic dissociation was detected in 71.4% of cases, PCR for SARS-CoV-2 negative in all 15 tested patients, and anti-ganglioside antibodies positive in 43.7%. Based on neurophysiology, 81.8% of patients had a diagnosis of AIDP diagnosis, 12.1% AMSAN and 6% AMAN. 29 patients have been treated with intravenous Immunoglobulin (IVIg), two with plasma exchange (PE), two with PE followed by IVIg and five untreated. The course was favorable in 76.3% of patients, stable in 10.5%, while 13.1% worsened, of which three died. The estimated occurrence rate in Lombardia is 0.5 GBS cases per 1000 COVID-19 infections.

Conclusion: We detected an increased incidence of GBS in COVID-19 patients which can reflect higher risk of GBS in COVID-19 patients or be secondary to an increase of prevalence of prior infection in that period.

Disclosure: Nothing to disclose

OPR-058

Clinical, neurophysiological and neuroradiological characteristics of SARS-Cov-2 encephalitis in Lombardia

F. Martinelli Boneschi [1], M. Sessa [2], D. Guidetti [3], G. Grampa [4], E. Magni [5], M. Versino [6], C. Ferrarese [7], D. Zarcone [8], A. Prelle [9], G. Micieli [10], C. Zanferrari [11], F. Frediani [12], A. Cagnana [13], A. Zilioli [14], M. Calloni [15], E. Mariani [16], C. Foresti [2], M. Crabbio [5], I. La Spina [17], A. Giorgetti [9], A. Cavallini [18], M. Ranieri [11], E. D'Adda [13], A. Salmaggi [19], A. Colombo [20]

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Background and aims: The number of cases of encephalitis in COVID-19 is increasing. We describe characteristics and outcome of encephalitis in COVID-19 (COV-ENC) patients in one of the most affected regions by COVID-19 of the world, Lombardia.

Methods: A multi-center observational study on neurological complications in COVID-19 patients was conducted by the Italian society of Hospital Neuroscience (SNO). Adult patients admitted to 20 Neurological units in Lombardia between February-April 2020 with COV-ENC have been included.

Results: 30 COV-ENC patients had a mean age of 66.5 years and male frequency of 56.6%. Altered consciousness was characterized by confusion in 86%, coma in 30%, delirium in 37.9% and alteration of personality trait in 27.6%. Epileptic seizures occurred in 74% of cases. One third of cases had hyperproteinorrachia, 1/3rd pleocytosis/hyperproteinorrachia, and left third had normal CSF. PCR for SARS-CoV-2 was negative in all tested patients. EEG was altered in 82.7% of patients. Brain CT and MRI were normal in nine patients, among abnormal findings nine patients had mesial temporal lesions, one of which confirmed with PET imaging. The course was favorable in 39.2% of patients, sequelae were few in 26.6% and moderate in 19.2%, while 20% of patients died.

Conclusion: The outcome tends to be worse in male patients. PCR negativity seems to confirm an autoimmune etiology more than a direct invasion of the virus. However, temporal lobe involvement, detected in 30% of patients with COV-ENC, suggest usual site of encephalitis due to herpes virus.

Disclosure: Nothing to disclose

Epilepsy: Quality of life, pregnancy and developmental outcomes

OPR-059

Epilepsy and depression – a bidirectional relationship

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Background and aims: Epilepsy and depression are two serious brain disorders that often co-occur, and the relationship between them has been suggested to be bidirectional; however, studies have provided ambiguous results, and the nature of the association between these two disorders remains to be fully understood.
Methods: In a nation-wide register-based cohort study, we identified all individuals who received a first diagnosis of epilepsy or depression from 1 Jan 1980 to 31 Dec 2016. For each person with epilepsy and depression we matched five persons without epilepsy and depression on age and sex at time of first diagnosis in the index person. We used Cox-regression to estimate the risk of epilepsy after depression and the risk of depression after epilepsy, adjusting for Charlson Comorbidity Index, substance abuse, and calendar time.
Results: In a population of 8,685,430 individuals, we identified 143,482 persons with epilepsy (54% males) with a median age at diagnosis of 42 years (interquartile range 17–65 years), and 226,149 persons with depression (37% males) with a median age at diagnosis of 43 years (interquartile range 29–60 years). The adjusted HR of depression after an epilepsy diagnosis was 1.91 (95% CI: 1.85–1.98) compared to persons without epilepsy, and the adjusted HR of epilepsy after a depression diagnosis was 2.37 (95% CI: 2.29–2.47) compared to persons without depression.
Conclusion: The risk of epilepsy is increased in persons with depression and the risk of depression is increased in persons with epilepsy. The results suggest a bidirectional association between depression and epilepsy and warrant further studies.
Disclosure: This project was conducted as a part of the "Braindrugs" project, funded by the Lundbeck Foundation. This work was supported by the Novo Nordisk Foundation (NNF16OC0019126), Central Denmark Region, and the Danish Epilepsy Association.

OPR-064

Longitudinal reduction of quality of life in patients with epilepsy and no seizure increase during the COVID-19 pandemic

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Background and aims: In early 2020, the novel coronavirus disease (COVID-19) pandemic has impaired medical care of chronic neurological diseases, including epilepsy. The objective of this study is to evaluate the impact of the COVID-19 pandemic in the levels of anxiety, depression, somnolence and quality of life using validated scales in patients with epilepsy in real-life clinical practice.
Methods: Self-administered scales of anxiety disorders (GAD-7), depression (NDDI-E), somnolence (Epworth Sleepiness Scale; ESS) and quality of life (QOLIE-31-P) in patients with epilepsy treated in the Refractory Epilepsy Unit of a tertiary hospital were longitudinally analyzed with Generalized Linear Mixed Models. Data were collected before the beginning (December 2019–March 2020) and during the COVID-19 pandemic (September 2020–January 2021).
Results: 37 patients, 45.0±17.3 years of age, 43.2% women, epilepsy duration 23.0±14.9 years, number of anti-epileptic drugs 2.1±1.4, answered in the two periods. Significant longitudinal reduction of QOLIE-31-P scores (from 58.9±19.7 to 56.2±16.2, p=0.035) was identified. No statistically significant longitudinal changes in NDDI-E (from 12.3±4.3 to 13.4±4.4, p=0.293) or the number of seizures (from 0.9±1.9 to 2.5±6.2, p=0.125) were found. Significant higher ESS (from 4.9±3.7 to 7.4±4.9, p=0.001) and lower GAD-7 scores (from 8.8±6.2 to 8.3±5.9, corrected p=0.024 adjusted by refractory epilepsy and sleep disturbance) were found during the COVID-19 pandemic.
Conclusion: During the COVID-19 pandemic, quality of life was lower in patients with epilepsy, levels of anxiety were reduced and sleepiness levels were raised, without seizure change. Additional studies would be useful to adequately manage these comorbidities.
Disclosure: There is no disclosure.

OPR-151

Impact of fatigue on health-related quality of life in patients with drug-resistant focal epilepsy

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Background and aims: Improvement of health-related quality of life (HRQoL) is considered a main goal of treatment of drug-resistant focal epilepsy (DRFE). HRQoL is believed to be a complex parameter with multiple disease- and patient-specific determinants.
Methods: 111 adult patients with DRFE were included in the study. HRQoL was measured using the "Quality Of Life In Patients with Epilepsy – 31" questionnaire (QOLIE-31). The severity the disease (frequency and subjective assessment of the severity of attacks), the effect of pharmacotherapy (drug load and composition of the treatment regimen), the social status of patients, comorbidities (anxiety, depression, fatigue) were assessed.
Results: The median of the final score for QOLIE-31 was 65.4 (interquartile range – 53.0–72.6 points). A statistically significant decrease in HRQoL was found in subgroups of patients with seizures during the previous three months, taking carbamazepine or barbiturates, suffering from anxiety and depressive disorders, with fatigue, as well as in unemployed patients ($p>0.05$). A multiple linear regression model ($R2=0.66$) was developed, which included the following determinants: Fatigue Severity Scale (=-0.612), Liverpool Seizure Severity Scale (=-0.159), and the risk of depression according to the NNDI-E questionnaire (=-0.174).
Conclusion: Pathological fatigue has a large negative impact on HRQoL along with seizure severity perception and depression. These factors need to be addressed in clinical practice in order to improve HRQoL.
Disclosure: This study was supported by RFBR grant 18-013-00222.

OPR-154

Prenatal antiseizure medication exposure and risk of autism and intellectual disability.SCAN-AED: a Nordic cohort study

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Background and aims: The objective of this study was to investigate the risk of autism spectrum disorder (ASD) and intellectual disability (ID) after prenatal exposure to antiseizure medication (ASM).
Methods: We carried out a population-based cohort study (www.scanaed.org) of singleton births using linked health and social register data from Denmark, Finland, Iceland, Norway, and Sweden. We defined prenatal exposure by ASMs prescription fills from 90 days before pregnancy to birth and child outcomes by ICD-10 codes from specialist healthcare. Cox regression provided hazard ratios (HR) for ASD and ID in children after prenatal exposure to the 10 most common ASM monotherapies We adjusted for potential confounders using fine strata propensity score weighting.
Results: We identified 4,493,377 singleton births with a median

follow up of eight years (interquartile range 4.0–12.1. Background characteristics Table 1). Compared with unexposed children, ASM exposed children (0.7%) had an increased risk of ASD and ID with highest estimates for valproate and topiramate. For valproate (n=3,042) the adjusted HR (95% confidence intervals) was 2.9 (1.5-5.7) for ASD, and 4.3 (3.5–5.3) for ID. For topiramate (n=879) the adjusted HRs were 2.8 (1.9–4.2) and 3.3 (2.3–4.6) respectively. The associations between prenatal exposure to other ASMs and neurodevelopmental outcomes were weaker and disappeared when we accounted for maternal disease by comparing exposed and unexposed children among mothers with epilepsy.

Table 1: Characteristics of study population according to prenatal exposure to antiseizure medication (ASM) [1]

	No ASM	Any ASM
Pregnancies, n	4 462 358	31 019
Characteristics of mothers		
Maternal age, mean (sd)	30.2 (5.2)	30.2 (5.4)
Parity, n (%)		
0	1 920 451 (43.0)	14 532 (46.9)
1	1 599 692 (35.9)	9 562 (30.8)
≥ 2	919 501 (20.6)	6 723 (21.7)
Missing	22 713 (0.5)	202 (0.65)
Married/cohabiting, n (%)		
no	329 965 (7.4)	4 418 (14.2)
yes	4 052 347 (90.8)	26 030 (83.9)
Missing	80 045 (1.6)	80 (0.3)
Education, n (%)		
Compulsory	611 126 (13.7)	7 618 (24.6)
Secondary/Pre-university	2 073 541 (46.5)	14 901 (48.0)
Bachelor	978 623 (21.9)	5 111 (16.5)
Master/PhD	614 053 (13.8)	2369 (7.6)
Missing	185 014 (4.2)	1 020 (3.3)
Antidepressants LMP-90 to birth, n (%)	156 881 (3.5)	7 842 (25.3)
Opioids LMP-90 to birth, n (%)	165 503 (3.7)	4 839 (15.6)
Epilepsy[2], n (%)	8862 (0.2)	15 750 (50.8)
Depression, n (%)	59 023 (1.3)	3 378 (10.9)
Anxiety, n (%)	96 178 (2.2)	4 176 (13.5)
Personality disorder, n (%)	14 148 (0.3)	19 57 (6.3)
Bipolar disorder[2] , n (%)	5 956 (0.1)	3079 (9.9)
Number of chronic somatic diseases[4], n (%)		
0	4 118 321 (92.3)	27 014 (87.1)
1	321 213 (7.2)	3 567 (11.5)
≥ 2	22 824 (0.5)	438 (1.4)
Number of pre-pregnancy hospitalizations the last year before pregnancy[5], n (%)		
0	3 785 855 (84.8)	23 223 (74.9)
1	558 191 (12.5)	4 922 (15.9)
≥ 2	118 312 (2.7)	2 874 (9.3)
Characteristics of children		
Male, n (%)	2 290 256 (51.3)	15 911 (51.3)

1) Exposure to antiseizure medication (ASM) defined as filling ASM prescriptions between 90 days before last menstrual period to delivery. 2) Diagnosis in the prescription -and birth registers and/or in records from specialist heath care the last year be

Conclusion: In this very large nationwide study from five Nordic countries, prenatal valproate and topiramate exposure were associated with increased risk of autism and intellectual disability.

Disclosure: Supported by NordForsk and the Research Council of Norway. Bjørk and Christensen report fees from Novartis,Eisai and UCB, and Bjørk,Zoega,Igland and Tomson institutional funding from Sanofi, Novartis, AbbVie, Eisai, Sandoz, Sun UCB, Bial, GSK, Teva.

OPR-185

Prenatal exposure to antiseizure medication and the full spectrum of diagnosed psychiatric disorders: A SCAN-AED study

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Background and aims: We examined the association between prenatal exposure to antiseizure medication (ASM) with psychiatric disorders among children of mothers with epilepsy.

Methods: We carried out a prospective population-based register study within the SCAN-AED project (www.scanaed.org), based on children born in Denmark, Finland, Iceland, Norway and Sweden between 1996 and 2016. Maternal use of ASM in pregnancy was defined as any redeemed prescription of ASM from 90 days before pregnancy to birth and assessment of psychiatric disorders in children was based on ICD-10 diagnoses (F10-F99) from specialized care. Maternal epilepsy was defined as any hospital contact with epilepsy or use of ASM with epilepsy as indication from one year before pregnancy to birth. Adjusted hazard ratios (aHR) and 95% confidence intervals (CIs) were estimated using Cox proportional hazard models.

Results: From the overall SCAN-AED population consisting of 4,490,152 live-born singletons, we identified 25,288 (0.6%) children of mothers with epilepsy, of whom 15,899 (62.9%) were prenatally exposed to ASM. Compared with children of mothers with epilepsy who did not use ASM during pregnancy, we found an increased risk of psychiatric disorders with prenatal exposure to valproate (aHR=1.85, 95% CI: 1.62–2.13) and topiramate (aHR= 1.43, 1.00–2.05), but not with lamotrigine, levetiracetam, carbamazepine, oxcarbazepine, clonazepam, and gabapentin. Prenatal valproate exposure was associated with increased risks of neurodevelopmental- and attachment disorders, but not with e.g. anxiety-, mood- and schizophrenia spectrum disorders.

Conclusion: In pregnant women with epilepsy, treatment with valproate and topiramate was associated with an increased risk of early-onset psychiatric disorders in the child.

Disclosure: This work was supported by the NordForsk Nordic Program on Health and Welfare (Project #83796), the Novo Nordisk Foundation (NNF16OC0019126), the Central Denmark Region, and the Danish Epilepsy Association.

OPR-187

Evaluation of Clinical Support and Medication Adherence of Women with Epilepsy During Pregnancy

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Background and aims: Women with epilepsy (WWE) have higher rates of mortality and morbidity during pregnancy. Reasons are unclear but a reduction in anti-seizure medication (ASM) levels and poor adherence to ASMs are likely relevant. This study aims to evaluate adherence to ASMs and access to specialist care for WWE during pregnancy.

Methods: Pregnant WWE within NHS Greater Glasgow and Clyde health-board were identified from the National Obstetric Register between June 2019–June 2020. A manual review of electronic patient records was undertaken to ensure diagnostic accuracy. Contact with epilepsy services was recorded. Medication dispensing records were obtained and a medication possession ratio to ASMs, six months before and after midwifery booking date, calculated.

Results: 87 WWE were identified: 43 with generalised (49.4%), 34 focal (39.1%) and 10 unclassified (11.5%) epilepsy. 42/87 WWE (48.3%) had input from epilepsy services within a year of conception. As of December 2020, 65/87 (74.7%) had antenatal input from epilepsy services, with 4/87 (4.6%) reviewed post-partum. One was pending review. No review was planned for 17/87 (19.5%). Of those reviewed, 21/65 (32.3%) were seen in the first trimester, 29/65 (44.6%) in the second and 15/65 (23.1%) in the third. Only 71/87 WWE were on ASMs. 32/71 (45.1%) had poor adherence to at least one of their ASMs before booking and 29/71 (40.8%) after booking.

Conclusion: National electronic databases demonstrate high incidence of non-adherence prior to and during pregnancy. Access to routine health-data and early review by specialist epilepsy services will provide opportunity to improve adherence and pregnancy-related outcomes in WWE.

Disclosure: Educational Grant from UCB Pharmaceuticals

Headache and Pain 1

OPR-065

Vascular Compression in Trigeminal Neuralgia discloses Trigeminal root somatotopic organization

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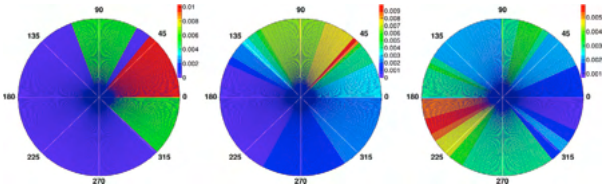
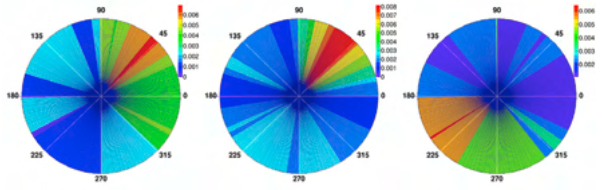
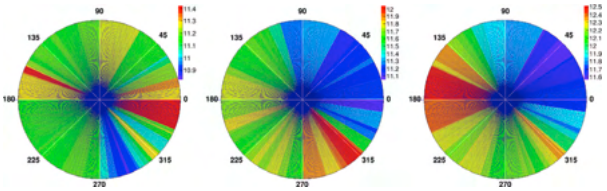
Background and aims: In Trigeminal Neuralgia pain is localized in the distribution of one or more branches of the trigeminal nerve. A hallmark of TN is the presence of discrete skin areas able to trigger pain attacks when touched. In classical TN trigeminal reflexes are normal but it is possible to recognize a vascular compression with morphological changes of trigeminal nerve root.
Methods: We enrolled 53 patients with clinically defined TN, normal trigeminal reflexes testing, and evidence of neurovascular compression at 3-Tesla MRI. From MRI images we measured the polar coordinates of the impacting vessel on the trigeminal root circumference and then correlate it with pain distribution, trigger zones and latencies of the early components of the trigeminal reflexes.
Results: Pain in V1, V2 and V3 is associated, respectively, with vascular compression in the medial, superior and lateral aspect of the nerve ($p<0.05$). Cutaneous trigger zones are associated with corresponding region of the circumference ($p<0.05$). Increased latency of the R1 component of the blink reflex is associated with medial compression, while increased latency of the SP1 component of the masseter inhibitory reflex is associated with inferomedial compression when the reflex is evoked from the infraorbital nerve, and with lateral compression when it is evoked from the mental nerve ($p<0.05$).



Preliminary data of location of neurovascular compression along the root circumference as derived by MRI data of 25 TN patients with pain limited to one trigeminal division, three with pain in V1, 10 with pain in V2 and 12 with pain in V3. Patients with pain



Preliminary data of location of neurovascular compression along the root circumference as derived by MRI data of 31 TN patients reporting as cutaneous trigger zones forehead, cheek or jaw. Polar coordinates are expressed in degrees, with 0 corresponding t



Preliminary data of location of neurovascular compression along the root circumference as derived by MRI data of 45 TN patients that underwent complete trigeminal reflex testing. Polar coordinates are expressed in degrees, with 0 corresponding to the medi

Conclusion: Our study showing that pain distribution, trigger zones and increased latencies of the early components of the trigeminal reflexes are correlated with specific sites of neurovascular compression along trigeminal root circumference discloses its somatotopic organization.
Disclosure: Nothing to disclose.

OPR-066

Migraine in pregnancy and post partum-epidemiological and clinical characteristics

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Background and aims: Migraine is one of the most prevalent and disabling neurological disorders. The aim of our study was to assess whether women suffering from migraine are at increased risk of developing pregnancy and postpartum complications, and to evaluate their characteristics and medical needs.
Methods: Pregnancy and delivery records from a database of "Clalit" Health Medical Organization, Israel were reviewed. The diagnosis of migraine was based on the International Headache society criteria and ICD-9 codes. The study included a total of 161,574 women who gave birth during a time period of five years (2014–2019). The information collected included: demographic data, mode of delivery, medical and obstetric complications in each pregnancy trimester, use of medications and repeated medical consultations.
Results: 8,723 women had a diagnosis of migraine. The control group included the remaining 152,851 women. The risk of obstetric complications and postpartum depression were higher in migraine patients compared with the control group. Migraine pregnancies had increased risk of preeclampsia and stroke. There was an increased incidence of cesarean section (20.5% vs 18.1%) and epidural anesthesia (43.6% vs 36.5%). Women with migraine showed tendency to seek more medical consultations and use more medications during pregnancy and post-partum.
Conclusion: Pregnant women with migraine were at increased risk of having obstetric and medical complications compared with unaffected women, therefore should be included in a high-risk pregnancy protocol of care throughout pregnancy. We recommend a neurological follow-up during the pregnancy and post-partum period.
Disclosure: Nothing to disclose.

OPR-067

Occipital nerve stimulation in drug-resistant chronic cluster headache: a third-level hospital experience

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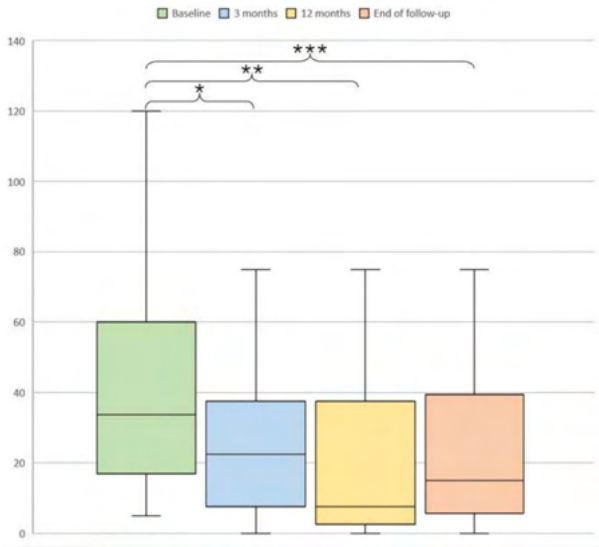
Background and aims: Occipital nerve stimulation (ONS) is a surgical treatment proposed for drug-resistant chronic cluster headache (drCCH). Long-term series assessing its efficacy are scarce.
Methods: We designed a retrospective observational study with consecutive sampling, evaluating the follow-up of 22 drCCH patients who underwent ONS. Our endpoint was the weekly attacks reduction. We also evaluated the pain intensity scored by the Visual Analogue Scale (VAS), patient overall perceived improvement and decrease in oral medication intake.
Results: After a median follow-up of 5.0 years, patients decreased from a median of 30 weekly attacks to 22.5 at three months [p=0.012], 7.5 at one year [p=0.006] and 15.0 at the end of follow-up [p=0.023]. The VAS decreased from a median of 10.0 to 9.0 at three months [p=0.011] and 7.0 at one year [p=0.002] and at the end of follow-up [p=0.002]. 23.5% had an overall perceived improvement of 70% at three months, 41.2% at one year and 27.8% at the end of follow-up. Reducing prophylactic oral medication was possible in 59.1% and it was stopped in 13.6%. Triptan use decreased in all the responder patients and 13.6% stopped its intake. 40.9% presented mild adverse events.



Evolution of weekly number of cluster headache attacks at baseline and after occipital nerve stimulation. Median and ranges are shown. *: p=0.012, **: p=0.006, ***: p=0.023

Conclusion: Our long-term experience shows that ONS is a beneficial treatment which does not entail serious harm and should be offered as the first option for drCCH management.
Disclosure: Financial support for medical writing were provided by Boston Scientific. The funder was not involved in the study design, collection, analysis or interpretation of data.

OPR-068

The effects of great occipital nerve block over photophobia in migraine patients

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Background and aims: To study the effect of greater occipital nerve (GON) block over photophobia in patients with migraine.
Methods: This is an observational prospective case-control study. Patients with migraine and photophobia attending the Headache Unit of a third-level hospital were recruited. Cases were defined as patients receiving GON block, which was performed at visit 1 (V1). All patients were evaluated with the Hospital Anxiety and Depression Scale, the Migraine Specific Quality of Life Questionnaire, the Utah Photophobia Symptom Impact Scale (UPSIS-12) and the Korean Photophobia Questionnaire (KUMC-8); both in V1 and one week after (V2).
Results: 41 patients were recruited; 28 cases and 13 controls. At V1, there were not significant differences in UPSIS (mean±SD): cases 29.4±8.3 vs controls 27.8±8.1, p=0.558) and KUMC-8 (cases 6.7±1.2 vs controls 6.2±1.7, p=0.323. At V2, cases experimented a significant improvement in photophobia impact scales compared to controls (UPSIS-12: reduction of 6.0±6.5 points, p<0.001; KUMC-8: reduction of 1.2±1.8 points, p=0.002). The other used scales did not show significant variation. Lesser improvement was seen in migraine with aura, but this was not statistically significant (reduction of 4.4±4.1 vs 8.5±8.7, p=0.101).
Conclusion: GON block has a beneficial effect over photophobia in migraine patients, measured with UPSIS-12 and KUMC-8. Patients without aura may have a greater improvement. GON block could be a useful therapeutic technique for photophobia in migraine.
Disclosure: The authors declare no conflict of interests.

OPR-069

Potential migraine "protectors": factors associated with decreased attack risk in individuals

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Background and aims: In the management of migraine, potential protective factors have been widely ignored even though they are probably as important as trigger factors. Therefore, the objective of this study was to identify factors associated with decreased migraine attack risk in individuals with migraine.
Methods: Individuals with migraine registered to use N1-Headache® and for 90 days entered daily data about potential attack risk factors (diet, mood etc), as well as migraine symptoms when these occurred. Univariate associations between each factor and migraine events were evaluated using Cox Proportional Hazards models. A factor was defined as a potential "protector" if significantly associated with a decreased risk of migraine attack (unadjusted hazard ratio <1; p-value <0.05).
Results: Out of 672 individuals included in this study (88% female; mean (SD) 8.8 (5.5) migraine days/month; 83% episodic migraine), no "protectors" were found in 211 (31.4%); 443 individuals (65.9%) had between one and eight "protectors"; and 18 (2.7%) had nine "protectors" or more. In a Day -1 analysis (excluding factor data on the day headache starts) fewer "protectors" were found: none in 314 individuals (46.7%), between one and five "protectors" in 339 (50.4%), and 19 had six "protectors". The most common "protectors" were waking feeling refreshed, feeling happy, good sleep quality, being relaxed and coffee/caffeine.
Conclusion: In two-thirds of individuals with migraine, at least one factor associated with decreased migraine attack risk could be identified. Knowledge of these factors may help individuals adopt behavioural changes that may, ultimately, decrease migraine attack risk.
Disclosure: SD, MV-M and GB are consultants to and hold stock options in Curelator Inc., AM is CEO of Curelator Inc. and holds stock and stock options in Curelator Inc., CW is a paid consultant to Curelator Inc.

OPR-070

Triptans and vascular comorbidity in over-fifties: Findings from a nationwide insurance database

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Background and aims: Beyond the age of 50, migraine is still common, and the incidence of vascular disorders increases. Triptans, specific drugs for acute migraine attacks, are vasoconstrictive and contraindicated in persons with vascular disorders. We aimed to gather the prescription of triptans and to evaluate whether vascular comorbidity differs in users and non-users of triptans over the age of 50.
Methods: Based on a nationwide insurance database from 2011, we compared the prescription of vascular drugs, vascular diagnoses (based on ATC-codes and ICD-10) and hospitalizations between triptan users >50 years and a control-group matched for age, sex, and place of residency.
Results: Of 3,116000 persons over 50, 13,833 (0.44%, 81% female) had at least one triptan prescription. 30% of the triptan users were over 50. In triptan-users, prescriptions of cardiac therapies and betablockers were significantly more common and prescriptions of calcium channel blockers and renin/angiotensin inhibitors were significantly less common. The prescriptions of antihypertensive, diuretic, and antilipidemic drugs, of platelet inhibitors and vitamin-K-antagonists, the frequency of vascular diagnoses, the number of hospital stays and of days in hospital did not differ significantly between the two groups.
Conclusion: In over-fifties, prescription of triptans is common. Even though triptans are contraindicated in vascular disorders, vascular comorbidity does not differ in users and non-users of triptans. Triptan users over the age of 50 should regularly be evaluated for vascular disorders and risk factors for such disorders. Future studies should assess the risk of triptan use in patients with vascular disorders.
Disclosure: Nothing to disclose.

OPR-071

Resting State Functional Connectivity Changes of the Pons in Migraine Patients: A Cross-Sectional and Longitudinal Study

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Background and aims: Previous studies support a key role of the dorsal pons in in migraine pathophysiology. In this study, we aimed to explore cross-sectional and longitudinal resting state functional connectivity (RS FC) changes of the pons in migraine patients.
Methods: Using a 3.0 Tesla scanner, RS functional magnetic resonance imaging (MRI) and 3D T1-weighted scans were acquired from 91 headache-free episodic migraine patients and 73 controls. Twenty-three migraineurs and 23 controls were reexamined after four years. RS FC analysis was performed using a seed-region correlation approach and SPM12.
Results: At baseline, compared to controls, migraine patients showed a decreased RS FC between the left pons and ipsilateral lingual gyrus and bilateral cerebellum. The left pons had also an increased RS FC with the left precuneus and bilateral orbitofrontal cortex. While, the right pons had a decreased RS FC with the left cerebellum, right fusiform and right inferior temporal gyrus. After four years, compared to controls, migraine patients developed a decreased FC between the left pons and the bilateral precuneus. The decreased RS FC between the left pons and ipsilateral cerebellum was associated to less severe and less frequent migraine attacks over the years.
Conclusion: Migraine patients experience altered functional interactions between the pons, pain and visual processing areas. A decreased RS FC between the pons and cerebellum might reduce the frequency and severity of migraine attacks over time. RS FC between the pons and precuneus, a region known to play a role in sensory integration, is initially strengthen, but weaken over time.
Disclosure: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Movement disorders: Neuroimaging

OPR-073

Motor cerebro-cerebellar networks breakdown among different subtypes of Parkinson's disease

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Background and aims: To investigate functional alterations in the cerebro-cerebellar system in two Parkinson's disease (PD) clinical phenotypes (tremor-dominant [TD] and postural instability and gait disorder [PIGD]) using stepwise functional connectivity (SFC).
Methods: 58 PD patients performed clinical and cognitive evaluations and resting-state functional MRI (fMRI). PD cohort was divided into two groups: 32 patients with TD (PD-TD) and 26 with PIGD (PD-PIGD). 60 age- and sex-matched healthy controls were also enrolled. SFC analysis aims to characterize regions that connect to specific seed brain areas at different levels of link-step distances. The cerebellar seed-region was identified using motor task-based fMRI in 23 controls. For each of the SFC maps, whole-brain two-sample t-test comparisons between groups were performed.
Results: The performance of the motor task during fMRI was associated with activation of the lobule VI and vermis of the cerebellum. SFC analysis at one-link step distance showed, in both PD subtypes, a decreased regional–local connectivity between seed region and thalamus and parietal lobe relative to controls; across intermediate link-steps, a reduced connectivity was observed with frontal, parietal and occipital lobes. Only PD-PIGD patients showed lower connectivity at intermediate link-step distances between the seed-cerebellar region and sensorimotor areas. In addition, SFC pattern identified different localization of functional overconnectivity in frontal lobe in both PD groups: in inferior frontal gyrus and insula in PD-PIGD, and in orbitofrontal gyrus in PD-TD.
Conclusion: These findings highlight subtype-specific PD changes in cerebellar functional connectivity, providing novel insights into the pathophysiological mechanism potentially underlying different motor phenotypes.
Disclosure: Ministry of Education and Science Republic of Serbia (Grant #175090).

OPR-077

Longitudinal clinical, cognitive and neuroanatomical changes over five years in GBA-positive PD patients

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Background and aims: To study the 5-year disease course of Parkinson's disease (PD) patients with glucocerebrosidase mutation (GBA-positive) at diagnosis compared to PD noncarriers (GBA-negative), evaluating changes in clinical/cognitive outcomes, and structural MRI.
Methods: 10 GBA-positive and 20 GBA-negative PD at diagnosis underwent clinical, neuropsychological and brain MRI assessments at study entry and once a year for five years. At baseline and at the last visit, each group of patients was compared in terms of cortical thickness and subcortical volumes to a group of 22 age-matched healthy controls (HC). Clinical, cognitive and MRI features were compared between groups at baseline and over time.
Results: At baseline, GBA-positive and GBA-negative patients had similar clinical and cognitive profiles. Compared to GBA-negative and HC, GBA-positive patients showed cortical thinning of left temporal, parietal and occipital gyri. Over time, compared to GBA-negative, GBA-positive worsened significantly in motor and cognitive symptoms, and showed a greater pattern of bilateral cortical thinning involving also frontal cortices. After 60 months, compared to HC, GBA-negative PD patients showed a pattern of cortical thinning similar to that shown by GBA-positive at baseline. The two groups of patients showed similar patterns of subcortical volume loss over time.
Conclusion: Compared to GBA-negative patients, GBA-positive PD showed a greater and earlier cortical thinning which worsened over time. GBA-negative PD patients reached the pattern of cortical thinning of
GBA-positive at the baseline only after five years, reflecting a slower disease progression. This study highlights the importance of the early detection of GBA mutation in PD patients.
Disclosure: This study was supported by the Ministry of Education and Science of the Republic of Serbia (Grant #175090).

OPR-103

Associations between grey matter metabolism and dopaminergic and serotonergic systems degeneration in de novo PD

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Background and aims: Degeneration of the nigrostriatal dopaminergic (DA) and the raphe-thalamic serotonergic (SE) systems due to alpha-synuclein accumulation in the brainstem is one among the earliest changes observed in Parkinson's disease.

Methods: We assessed in 96 drug-naïve de novo Parkinson's disease patients (age 71.9±7.5; 59 males) the association between cortical metabolism and DA-SE deafferentation of either striatum or thalamus, and then we explored whether this association was mediated by either striatum or thalamus metabolism. We acquired brain FDG-PET images as a marker of neurodegeneration and 123I-Ioflupane Single Photon Emission Computed Tomography (123I-FP-CIT-SPECT, as a marker of dopaminergic impairment in the striatum as well as a proxy marker of serotoninergic deafferentation in the thalamus).

Results: We found that 123I-FP-CIT specific-to-non displaceable binding ratio (SBR) and glucose metabolism positively correlated one another in bilateral caudate, bilateral putamen and bilateral thalami. Moreover, using a voxel-wise approach, we observed a direct correlation between temporo-parietal cortical metabolism and caudate DA innervation, as well as a direct correlation between prefrontal metabolism and thalamus SE innervation. Lastly, we found that the effect of caudate 123I-FP-CIT SBR values on temporo-parietal metabolism was mediated by caudate metabolic values (percentage mediated 91%, p-value= 0.008), as well as that the effect of thalamus 123I-FP-CIT SBR values on prefrontal metabolism was fully mediated by thalamus metabolic values ($p<0.001$).

Conclusion: These data shed light on the impact of diffuse projection systems degeneration on cortical metabolism in Parkinson's disease as well as on their regional specificity.

Disclosure: MP: fees from Novartis, Merck and Biogen. DA: fees from Fidia SM: speaker Honoraria from Ge Healthcare. FN: fees from Roche Bial e G.E. Healthcare. All other authors report no conflicts of interest.

OPR-105

Functional MRI connectivity of the primary motor cortex in functional dystonia patients

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Background and aims: This study explores the functional connectivity (FC) of the primary motor (M1) cortex in functional dystonia (FD) patients relative to healthy controls, with a focus on different clinical phenotypes.

Methods: 40 FD patients (12 fixed [FixFD]; 28 mobile [MobFD]) and 43 healthy controls (14 young FixFD-age-matched [yHC]; 29 old MobFD-age-matched [oHC]) underwent resting state fMRI. A seed-based FC analysis was performed using bilateral M1 as regions of interest.

Results: Compared to controls, FD patients showed reduced FC between left M1 and left dorsal anterior cingulate cortex, and between right M1 and left M1, premotor/supplementary motor area (SMA), dorsal posterior cingulate cortex (PCC), and bilateral precuneus. Relative to yHC, FixFD patients showed reduced FC between M1 and precuneus bilaterally. Compared to oHC, MobFD patients revealed reduced FC between right M1 and left M1, premotor/SMA, dorsal-PCC, bilateral primary sensory cortices and parieto-occipital areas, and increased FC of right M1 with right associative visual cortex and bilateral ventral-PCC. FixFD patients, relative to MobFD, showed lower FC between the right M1 and right associative visual area, and bilateral precuneus and ventral-PCC.

Conclusion: This study suggests an altered brain FC of the motor circuit with areas involved in emotional processes and sense of agency in FD. FixFD patients showed FC abnormalities mainly in areas related to sense of agency, while MobFD in regions involved in sensorimotor functions (reduced FC) and emotional processing (increased FC).

Disclosure: Ministry of Education, Science, and Technological Development of the Republic of Serbia (project #175090).

OPR-107

Cortical sensorimotor representations remain normal in musicians' dystonia despite global deficit in dexterity

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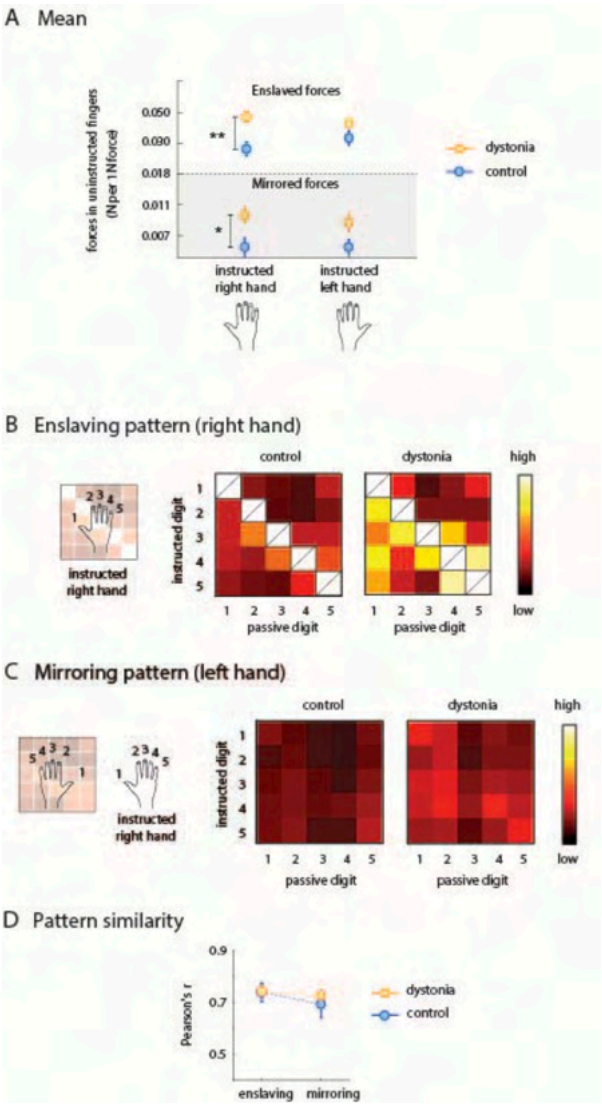
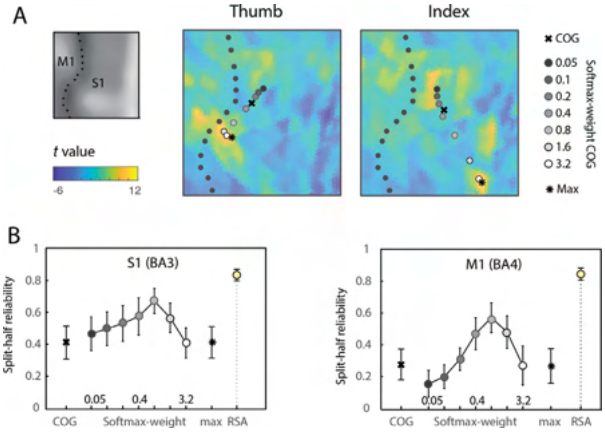
Background and aims: Musicians' dystonia presents with a persistent loss of motor control during musical performance. The predominant hypothesis is that this loss of motor control is underpinned by maladaptive neural changes to the somatotopic organization of finger representations in primary somatosensory cortex.

Methods: Here, we tested this hypothesis by investigating the finger-specific activity patterns in the primary somatosensory (S1) and motor cortex (M1) using functional magnetic resonance imaging with state-of-the art multivariate analyses in 11 musicians with dystonia and nine healthy musicians. We also characterized their dexterous finger control to investigate whether the deficit is strictly limited to musical performance or also generalizes to a non-musical task.

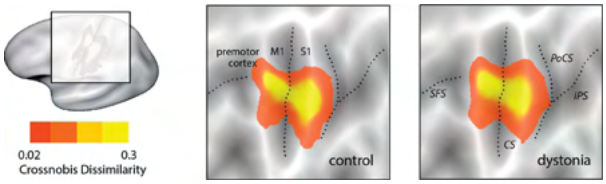
Results: We report two key findings. 1st, during the production of individuated finger presses, musicians with dystonia showed a small, but robust loss of motor control. This deficit was characterized by both a reduction in finger individuation ability, and an exaggeration of mirror movements primarily during use of the clinically identified symptomatic hand, but also to a lesser extent during asymptomatic hand use. 2nd, we found no evidence of disease-related changes in the corresponding finger representations in S1/M1.



Finger individuation was reduced in musicians with dystonia.



Comparison of different methods to characterize the spatial layout of digit representations.



Extent and location of digit representations for healthy musicians (controls) and musicians with dystonia.

Conclusion: Our results contradict the view that abnormalities in sensorimotor finger representations play a role in the pathophysiology of musicians' dystonia. Our behavioral results also suggest that the loss of finger dexterity in musicians' dystonia expresses along a spectrum with subtle abnormalities in motor control evident during ordinary dexterous tasks.
Disclosure: Nothing to declare.

OPR-146

The role of white matter hyperintensities in Parkinson's disease progression and outcome

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Background and aims: We aimed to investigate the influence of white matter hyperintensities (WMH) on the longitudinal progression and outcome in Parkinson's disease (PD).
Methods: 154 PD patients underwent clinical assessment, neuropsychological evaluation and Magnetic Resonance Imaging (MRI) scan once a year up to 48 months. WMH were identified on T2-weighted scans and WMH total volume was computed for each scan at baseline. Then PD patients were divided in subgroups: low (lowH, 25th quartile, n=45), intermediate (mediumH, between 25th and 75th quartile, n=77) and high (highH, 75th quartile, n=32) baseline WMH burden. Analysis of variance was used to compare groups at baseline and age-corrected linear regression models for longitudinal data. Influence of WMH on the progression to Hoehn & Yahr (H&Y) three and dementia was investigated with Kaplan-Meier estimator analysis (KM).
Results: Subjects in PD highH showed significantly lower scores in Mini Mental State Examination and Addenbrooke's Cognitive Examination compared to lowH, Longitudinally, the highH group showed a significant worsening in motor and non-motor variables ($p<0.001$) compared to lowH and mediumH, independent of the effect of age. The KM analysis showed lower rates of progression to dementia ($p=0.03$) and to H&Y score 3 ($p=0.02$) in the lowH group.
Conclusion: Our study showed that higher WMH volumes are associated with a worse progression of both motor and non-motor symptoms, independently from age. Moreover, PD patients with high WMH volumes are more likely to progress to dementia and to advanced disease stages in the following four years.
Disclosure: Ministry of Education and Science Republic of Serbia (Grant #175090).

OPR-149

Striatal Dopamine Transporter Imaging measures and CD4+ T cells profile in Parkinson's disease drug-naïve patients

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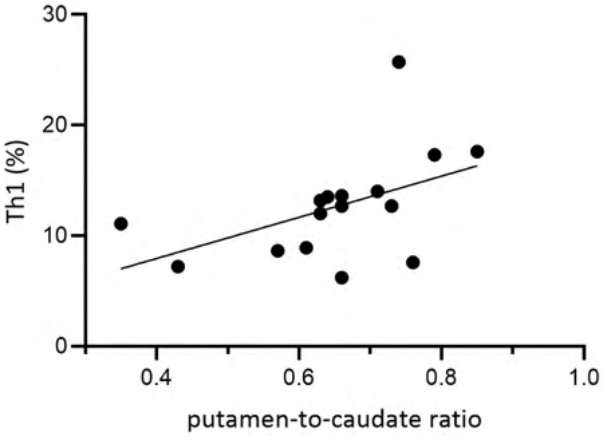
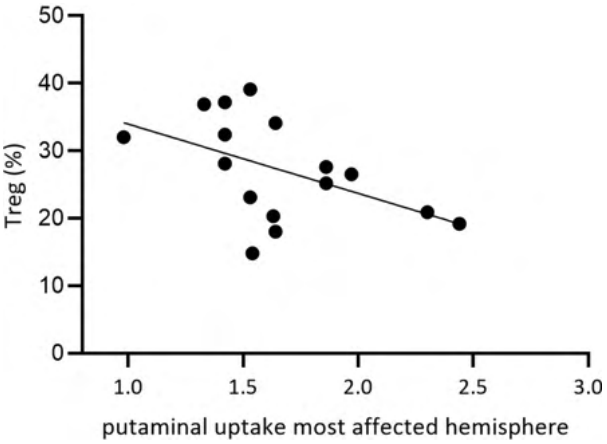
Background and aims: In Parkinson's disease (PD) there is a complex interplay between peripheral immunity and dopaminergic neural death in the nigrostriatal pathway. It has been found that in circulating CD4+ T lymphocytes from PD patients there are lower levels of Th2, Th17, and Treg subpopulations, with a relative increase of Th1, determining a pro-inflammatory bias. Nevertheless, no correlation with the quantitative assessment of dopaminergic neural loss in the striatal nuclei has been proved thus far.
Methods: 19 drug-naïve PD patients were enrolled, aged 65.84±7.8 years and with a mean UPDRS-III score of 11.38±4.7. A brain SPECT with [I-123]Ioflupane was performed, and automatic extraction of uptake at caudate and putamen level was conducted through the BasGan software. Within four weeks, a peripheral blood venous sample was obtained for CD4+T lymphocytes assessment. Th1, Th2, Th17, and Treg subsets were quantified using flow cytometry analysis. Expression of transcription factors genes TBX21, STAT1, STAT3, STAT4, STAT6, RORC, GATA3, FOXP3, and NR4A2 was measured by Real-Time PCR.
Results: In the most affected hemisphere an inverse correlation between putaminal uptake and percentage of CD4+ (r=-0.581, p=0.018) and Treg (r=- 0.560, p=0.024) was found. Total putamen-to-caudate ratio and striatal binding ratio showed respectively a direct correlation with percentage of Th1 (r=0.576, p=0.02) and an inverse correlation with percentage of CD4+ (r=-0.682, p=0.01).



Direct correlation between total putamen-to-caudate ratio and Th1 (%)



Inverse correlation between putaminal uptake and Treg (%)

Conclusion: To our knowledge, this is the first evidence highlighting a possible relationship between CD4+ T cells profile and DaTscan measures. Unbalanced levels of circulating Th1 and Treg subpopulations may be involved in the early stages of PD.
Disclosure: Nothing to disclose.

Miscellaneous: Infectious Diseases and Neuro-oncology

OPR-079

Anti-PD-L1 Treatment for Progressive Multifocal Leukoencephalopathy: Lessons from Two Cases

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Background and aims: Progressive multifocal leukoencephalopathy (PML) is a brain infectious disease caused by JC virus (JCV) in the course of cellular immunodeficiency. There is no effective anti-viral treatment for PML but immune restoration using immune checkpoint inhibitors (ICIs) recently emerged as a therapeutic hope.
Methods: We administrated atezolizumab, an anti-programmed death-ligand 1 antibody, at the dosage of 1,200 milligrams every three weeks to two patients with PML hospitalized at Liège University Hospital (Belgium). Follow-up consisted in weekly physical examination, cerebral magnetic resonance imaging (cMRI) and JCV polymerase chain reaction in the cerebrospinal fluid (CSF) every three weeks.
Results: Characteristics of both patients at baseline are summarized in Tab. 1. Patient 1 showed remarkable clinical improvement following treatment initiation, recovering the ability to walk with assistance and speak simple sentences. CSF JCV load reduced from 17,564 to 1,870 copies/ml (Fig. 1). Lesions visualized with cMRI stopped progressing (Fig. 2). After initial clinical and virological improvement (Fig. 1), patient two developed life-threatening immune reconstitution inflammatory syndrome (IRIS) with brutal clinical deterioration and status epilepticus. She received prolonged high-dose intravenous methylprednisolone resulting first in IRIS resolution but then in slow PML progression.

Patient	Sex	Age (yo)	Etiology of immune deficiency	CD4+; CD8+; CD19+ counts (number/mm³)	Clinical characteristics	JVC in CSF (copies /ml)
1	Man	66	○ Lung adenocarcinoma ○ Alcoholic liver disease ○ No previous iatrogenic immunosuppression	140; 210; 100	○ Global aphasia; no usable speech ○ Severe cerebellar ataxia ○ Right hemiparesis ○ Bedridden	17,564
2	Woman	77	○ B-cell chronic lymphocytic leukemia ○ Previous treatment with rituximab and chlorambucil	280; 80; 30	○ Motor aphasia; fragmentary expression ○ Cognitive impairment ○ Cerebellar ataxia ○ Bedridden	733,845

Tab. 1: Patients characteristics at baseline. M denotes man, W woman, yo year-old, JCV JC virus, CSF cerebrospinal fluid.

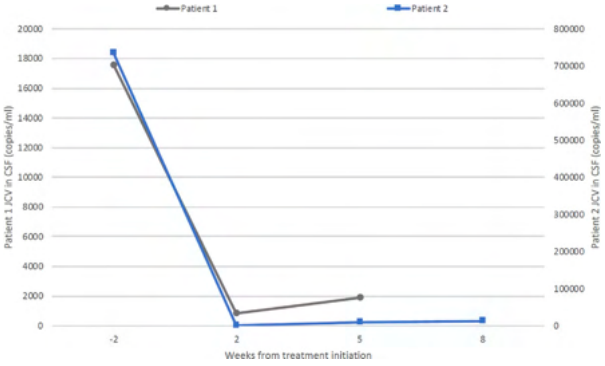

Fig. 1: Evolution of the JC viral load in the CSF during atezolizumab treatment

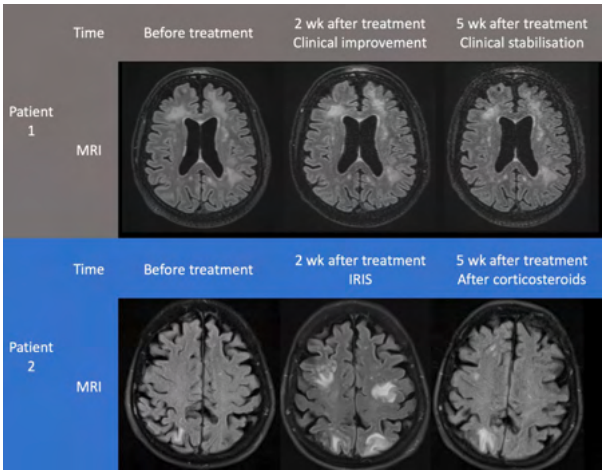

Fig. 2: Evolution of cerebral MRI scans (T2-fluid attenuated inversion recovery-weighted imaging) during atezolizumab treatment. Wk denotes weeks.

Conclusion: Atezolizumab successfully reinvigorated anti-JCV immunity in our two patients. It was also responsible for life-threatening IRIS in one patient. Since corticosteroids impair JCV-specific T-cell response and mitigate beneficial ICIs effects, methylprednisolone probably resulted in treatment resistance. ICI-associated PML-IRIS represents a particularly complex clinical situation during which deleterious consequences of IRIS have to be balanced with potential loss of treatment efficiency due to iatrogenic immunosuppression.
Disclosure: Atezolizumab was supplied by Roche on a compassionate use basis.

OPR-080

Neurofilament light chain in central nervous system infections: a prospective study of diagnostic accuracy

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Background and aims: Patients with suspected central nervous system (CNS) infections are often a diagnostic challenge. Neurofilament light chain (NfL), a component of the axonal cytoskeleton and an identified marker of neuronal damage, might be of diagnostic relevance for the diagnosis of CNS infections
Methods: We analyzed patients from a prospective cohort in the Netherlands in whom a lumbar puncture was performed for suspected CNS infection. The index test was NfL in CSF and the reference standard the final clinical and/or confirmed diagnosis.
Results: We included 273 patients, with a median age of 50 years (IQR 35-65) and 52% (n=142) were women. Patients were diagnosed with a CNS infection (26%, n=70), CNS inflammatory disease (7%, n=20), systemic infection without CNS involvement (32%, n=87), non-infectious or -inflammatory neurological disorders (33%, n=90) and other systemic diseases (2%, n=6). The median level of NfL was 593 pg/ml (IQR 249–1,569) and did not discriminate between diagnostic categories or CNS infection subcategories. The AUC for diagnosing a CNS infection was 0.50 (95% CI 0.42–0.59). The AUC for differentiating bacterial meningitis from a viral CNS infection was 0.65 (95% CI 0.50–0.81). Patients presenting with seizures, focal neurological deficits or altered mental status had higher NfL levels compared to other patients. NfL was associated with mortality and unfavorable outcome (odds ratio 1.16 [95% CI 1.08–1.24] and 1.14 [95% CI 1.06–1.22] per 1,000pg/ml).
Conclusion: NfL has no diagnostic value in patients suspected of CNS infections to discriminate between causes. High concentrations of NfL are associated with severe neurological disease and unfavorable outcome.
Disclosure: Nothing to disclose.

OPR-081

Abstract withdrawn

OPR-082

ABTR-SANO Real-World Pattern of Care Study on Glioblastoma in the Austrian Population. Update 2020.

S. Oberndorfer [1], A. Woehrer [2], C. Marosi [3], T. Urbanic-Purkart [4], M. Nowosielski [5], S. Iglseder [5], G. Stockhammer [5], W. Kleindienst [6], M. Stultschnig [7], B. Surböck [2], J. Pichler [8], S. Weiss [9], M. Hutterer [6], A. Hager [10], L. Seebrecht [11], T. Rötzer [11], A. Hainfellner [11], J. Hainfellner [2]
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Background and aims: The Austrian ABTR-SANO Glioblastoma Registry is the first population-based assessment of patterns of care for patients with Glioblastoma across Austrian healthcare institutions. The primary aim is to assess the real world effectiveness of administered therapies.
Methods: Clinical data are collected via a common web-based IT platform "ABTR-SANO Net" since 2014. The database and the ongoing evaluation of clinical parameters, as well as interims analysis are provided in cooperation with a review board.
Results: 11 centers across Austria are involved, which collect the information of now over 1,600 patients (m/f ratio: 1,3 – median age: 66 years). The proportion of patients with cross total resection increased gradually since 2014 from 36% to 56% in 2020. Almost all patients were MGMT testet in 2020, whereas in 2014 only half of patients underwent MGMT testing. Analysis of median time from clinical presentation to diagnostic scan (overall: nine days), time from diagnostic scan to surgery (overall: 10 days), and time from surgery to the beginning of first line treatment (overall: 31 days) was stable throughout the years. First overall survival data show a median survival of Austrian Glioblastoma patients of 12 months.
Conclusion: One defined set of clinical parameters results in excellent phenotypic annotation of the patient cohort from 2014 ongoing. Pattern of care characteristics show a different picture with respect to treatment, as we used to see in RCT. The first outcome analysis comparing different Austrian centers is available since 2020.
Disclosure: The project is funded by the Austrian Society of Neurology (ÖGN), ROCHE © and AbbVie©.

Multiple Sclerosis: Clinical studies

OPR-083

Safety of Ocrelizumab in Patients With RRMS With Suboptimal Response to Prior DMTs: Data From the CASTING Study

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Background and aims: Patients with relapsing-remitting multiple sclerosis (RRMS) often experience disease activity despite receiving a disease-modifying therapy (DMT). The Phase IIIb CASTING study (NCT02861014) evaluated the efficacy and safety of ocrelizumab in patients with RRMS who had a suboptimal response to ≥6 months' treatment with one or two prior DMTs. Here we evaluate CASTING 2-year safety outcomes by subgroups, including age and prior DMT.

Methods: Patients (n=680; Expanded Disability Status Scale score ≤4.0; discontinued prior DMT due to suboptimal response) received intravenous ocrelizumab 600mg every 24 weeks for 96 weeks. Safety outcomes included adverse events (AEs), serious AEs (SAEs), AEs ≥Grade 3, discontinuations for AEs, infections, serious infections (SIs), and lymphocyte count.

Results: Safety outcomes were comparable between subgroups by age or prior DMT (Tab. 1, 2). No haematological abnormalities were seen in patients treated with ocrelizumab, regardless of previous DMTs or age. A single death occurred in the study; this was suicide (not related) and occurred in a patient who had one prior DMT (teriflunomide), aged >40 years.

Table 1.

	One prior DMT (n=411)	Two prior DMTs (n=269)	Age <=40 years (n=511)	Age >40 years (n=169)
Percentage of patients with event				
AEs	89.3%	88.8%	88.8%	89.9%
SAEs	7.5%	6.7%	7.4%	6.5%
Infections	67.6%	65.8%	66.3%	68.6%
SIs	1.9%	1.1%	1.8%	1.2%
Discontinuations for AEs	1.2%	0.7%	1.4%	0
AEs >=Grade 3	12.9%	11.9%	11.4%	13.6%
Lymphocytes (x10⁹/L), median (range) at Week 96	1.60 (0.39–3.60)	1.57 (0.69–3.51)	1.60 (0.69–3.60)	1.50 (0.39–3.07)

Tab. 1

Table 2.

	Last DMT				
	Interferons (n=198)	Glatiramer acetate (n=116)	Dimethyl fumarate (n=168)	Teriflunomide (n=65)	Fingolimod (n=129)
Percentage of patients with event					
AEs	87.4%	89.7%	91.7%	92.3%	86.0%
SAEs	8.1%	9.5%	3.6%	12.3%	6.2%
Infections	66.2%	68.1%	69.0%	67.7%	62.8%
SIs	2.0%	0.9%	1.8%	3.1%	0.8%
Discontinuations for AEs	1.0%	1.7%	1.2%	1.5%	0
AEs >=Grade 3	11.6%	11.2%	11.9%	18.5%	10.1%
Lymphocytes (x10⁹/L), median (range) at Week 96	1.56 (0.39–3.30)	1.53 (0.70–3.60)	1.58 (0.79–2.97)	1.71 (0.80–3.21)	1.34 (0.69–3.10)

Tab. 2

Conclusion: The safety profile was comparable between subgroups, including age and number/type of prior DMTs. No new safety signals were identified.

Disclosure: Sponsored by F. Hoffmann-La Roche Ltd; writing and editorial assistance was provided by Articulate Science, UK.

OPR-084

Determination of a clinically effective evobrutinib dose: exposure-response analyses of a phase II MS study

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Background and aims: The pharmacometric analysis of this double-blind, randomised, phase II trial (NCT02975349) investigating the safety and efficacy of evobrutinib, explored exposure-response relationships and suitable dosing regimens of evobrutinib, a highly selective Bruton's tyrosine kinase (BTK) inhibitor, for relapsing multiple sclerosis.

Methods: Population pharmacokinetic (PK)/pharmacodynamic (PD) modelling was performed on data from fasted patients treated with placebo or evobrutinib (25mg once daily (QD), 75mg QD, or 75mg twice daily (BID)) for 24 weeks (W), followed by a 24W blinded extension (placebo patients switched to evobrutinib 25mg QD). Model-based exposures for PK and BTK occupancy (BTKO) were used for cross-sectional
exposure-response analyses (maximum n=207). Alternative dosing regimens were simulated.

Results: Exposure-response modelling indicated a relationship between evobrutinib exposure and clinical response for total T1 Gd+ and new/enlarging T2 lesions at W12 to 24, and annualized relapse rate (ARR) at W48. A steady state (SS) area under the curve over 24 hr of 468 and 400ng/mL*hr or higher appeared to be associated with lesion reduction and ARR improvement, respectively. These exposures were associated with SS predose BTKO of 95%. Based on PK and BTKO profile simulations, evobrutinib 75mg BID without food is predicted to maintain predose BTKO at SS of >95% in 92% of patients. Evobrutinib 45mg BID with food is predicted to achieve similar exposure as 75mg BID without food and provide predose BTKO of >95% in 93% of patients.

Conclusion: An evobrutinib dose of 45mg BID with food will be pharmacologically effective and is appropriate for clinical use in phase III multiple sclerosis trials.

Disclosure: This research was funded by Merck KGaA, Darmstadt, Germany.

OPR-085

Effect of Ocrelizumab on Cerebellar Atrophy in RMS and PPMS: Results from OPERA I/OPERA II and ORATORIO

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Background and aims: In multiple sclerosis (MS), the cerebellum is affected by lesions and secondary degeneration of connections with supratentorial brain and spinal cord. However, temporal cerebellar atrophy dynamics and treatment impact remain unclear. The aim is to assess ocrelizumab (OCR) effect versus interferon beta-1a (IFN)/placebo (PBO) on cerebellar atrophy in relapsing MS (RMS)/primary progressive MS (PPMS), in the phase III OPERA (NCT01247324/NCT01412333) and ORATORIO (NCT01194570) trials, respectively.

Methods: During the double-blind and open-label extension (OLE, all patients on OCR) periods of OPERA and ORATORIO, changes in cerebellar volume from baseline were computed using Jacobian integration and analysed using a mixed-effect repeated measurement model, adjusted for baseline volume, age, region (US vs rest of the world), Expanded Disability Status Scale category (<4, >=4), week, treatment, treatment-by-time interaction, treatment-by-baseline-volume interaction, gadolinium-enhancing lesions (presence/absence) and T2 lesion volume.

Results: In OPERA, changes in cerebellar volume (%) at Weeks 24, 48, 96, OLE Weeks 46, 94, 142, 190 and 238 were: -0.42/-0.27 ($p<0.001$), -0.58/-0.46 ($p=0.007$), -0.92/-0.63 ($p<0.001$), -1.08/-0.81 ($p<0.001$), -1.32/-1.02 ($p<0.001$), -1.48/-1.21 ($p<0.001$), -1.61/-1.34 ($p=0.004$) and -1.83/-1.63 ($p=0.05$) for IFN/OCR patients, respectively. In ORATORIO, changes (%) in cerebellar volume at Week 24, 48, 120, OLE Day 1, Week 48, 96, and 144 were: -0.24/-0.12 ($p=0.042$), -0.33/-0.29 ($p=0.493$), -0.83/-0.72 ($p=0.207$), -1.23/-1.06 ($p=0.150$), -1.58/-1.23 ($p=0.010$), -1.82/-1.53 ($p=0.064$) and -2.12/-1.77 ($p=0.043$) for PBO/OCR patients, respectively.

Conclusion: Compared with IFN, ocrelizumab reduced cerebellar atrophy in RMS. During the OLE, patients initially randomized to ocrelizumab maintained lower cerebellar volume loss relative to baseline in both RMS and PPMS.

Disclosure: The study was sponsored by F. Hoffmann-La Roche Ltd; writing and editorial assistance was provided by Articulate Science, UK.

OPR-086

Ublituximab versus teriflunomide in relapsing multiple sclerosis (RMS): Results of the Phase 3 ULTIMATE I and II trials

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Background and aims: Ublituximab (UTX) is a novel monoclonal antibody targeting a unique epitope on the CD20 antigen and is glycoengineered for enhanced B-cell depletion through antibody-dependent cellular cytotoxicity (ADCC). The increased ADCC may offer benefit over available anti-CD20 agents in terms of lower doses and shorter infusion times.

Methods: Patients were randomized (1:1) to receive either 450mg UTX via a one-hour intravenous infusion every 24 weeks (following day one infusion of 150mg) or 14mg oral teriflunomide once-daily, throughout a 96-week treatment period. Eligible patients had diagnosis of RMS (McDonald Criteria 2010), Expanded Disability Status Scale (EDSS) score of 0–5.5, and age of 18–55 years. The primary endpoint was annualized relapse rate (ARR). Key secondary endpoints include MRI, no evidence of disease activity (NEDA), confirmed disability progression and safety/tolerability

Results: Overall, 1,094 patients were randomized in 10 countries (ULTIMATE I, N=549; ULTIMATE II, N=545). Both studies met their primary endpoint of significantly reduced ARR ($p<0.005$ in each study) with UTX demonstrating an ARR of <0.10 in each of the studies. Reductions of approximately 60% and 50% in ARR over teriflunomide were observed in ULTIMATE I & II, respectively.

Conclusion: ULTIMATE I&II significantly reduced ARR ($p<0.005$ in each study) with UTX demorating an ARR of <0.10 in each of the studies, utilizing a one-hour 450mg ublituximab infusion every six months after the first cycle infusions in RMS. Additional efficacy/safety results will be presented at the meeting.

Disclosure: Authors have received compensation from Pharma companies for speaking, consulting and contracted research.

OPR-087

GFAP as a Marker of Disease in Relapsing Multiple Sclerosis: Post Hoc Analysis of the Phase 3 Ozanimod SUNBEAM Trial

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Background and aims: Glial fibrillary acidic protein (GFAP), an intermediate filament expressed by astrocytes, is involved in central nervous system (CNS) cell communication and blood-brain barrier function. GFAP may be a biomarker in various CNS conditions, including multiple sclerosis. This post hoc analysis explored relationships between baseline plasma GFAP concentration and patient and disease characteristics in the SUNBEAM trial (NCT02294058) of ozanimod in relapsing multiple sclerosis (RMS).

Methods: This randomised, double-blind trial compared oral ozanimod 0.92 or 0.46 mg/day with intramuscular interferon beta-1a 30 µg/week for 12 months in adults with RMS. GFAP was measured using Simoa® GFAP Assay (Quanterix, Billerica, MA). Using regression analysis, we investigated relationships between baseline GFAP and demographic and disease characteristics at baseline and month 12.

Results: Of 1,346 participants randomised, 1,117 had baseline GFAP assessments (median 113.03pg/mL). Men had lower baseline GFAP concentration than women ($R2=1.5\%$ for GFAP relationship with sex; $p=0.0002$). GFAP and age had a U-shaped relationship ($r2=1.3\%$; $p=0.0018$). GFAP related positively to plasma neurofilament light chain (NfL) concentration ($r2=19.8\%$) and inversely to body mass index (BMI) ($R2=5.5\%$; both $p<0.0001$). Baseline GFAP was unrelated to pretreatment relapse but higher in those with more relapses through month 12 ($r2=5.7\%$; $p<0.0001$). Baseline GFAP positively related to T2 and gadolinium-enhancing lesion counts and inversely related to whole brain volume (WBV) at baseline ($R2=4.7\%9.2\%$) and month 12 ($R2=5.0\%8.5\%$) (all $P<0.0001$).

Conclusion: We found significant but weak relationships between baseline GFAP and sex; age, BMI, and NfL concentration at baseline; lesion counts and WBV at baseline and on treatment; and on-treatment relapse.

Disclosure: This study was supported by Bristol Myers Squibb, Princeton, NJ.

OPR-088

Whole Brain, Cortical Grey Matter, and Thalamic Volume Changes During 3 to five Years of Ozanimod in Relapsing MS

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Background and aims: Ozanimod reduced whole brain volume (WBV), cortical grey matter volume (CGMV), and thalamic volume (TV) loss vs interferon beta-1a (IFN) in phase 3 SUNBEAM (NCT02294058) and RADIANCE (NCT02047734) trials. We evaluated brain volume loss among SUNBEAM/RADIANCE participants who entered an ongoing extension trial (DAYBREAK, NCT02576717).

Methods: The two randomised, double-blind trials compared oral ozanimod 0.92 and 0.46mg/day with intramuscular IFN 30 µg/week in adults with relapsing MS. Completers were eligible to receive open-label ozanimod 0.92mg/day in DAYBREAK. MRI was performed at months six (SUNBEAM), 12 (SUNBEAM/RADIANCE), and 24 (RADIANCE), then every 12 months (DAYBREAK). Baseline WBV and CGMV were measured using SienaX, and TV using ThalamicVolume software; percentage change in WBV, CGMV, and TV was quantified using Jacobian integration. Data are reported through DAYBREAK month 36.

Results: DAYBREAK includes 2257 SUNBEAM/RADIANCE participants. Loss of WBV (Fig 1A), CGMV (Fig 1B), and TV (Fig 1C) was less on ozanimod than IFN and remained less after switching from IFN to ozanimod, especially for WBV (Fig 1A) and TV (Fig 1C). CGMV was lost to a much greater extent while on IFN, and recovered substantially, but not completely, upon switching to ozanimod (Fig 1B).

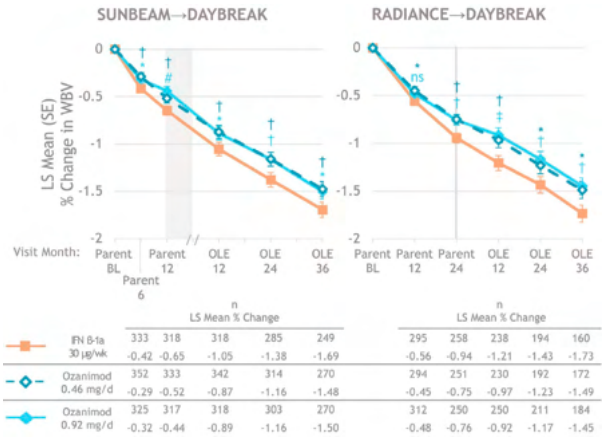

Figure 1. Mean (SE) Percentage Change From Baseline in (A) Whole Brain Volume, (B) Cortical Grey Matter Volume, and (C) Thalamic Volume; (A) WBV

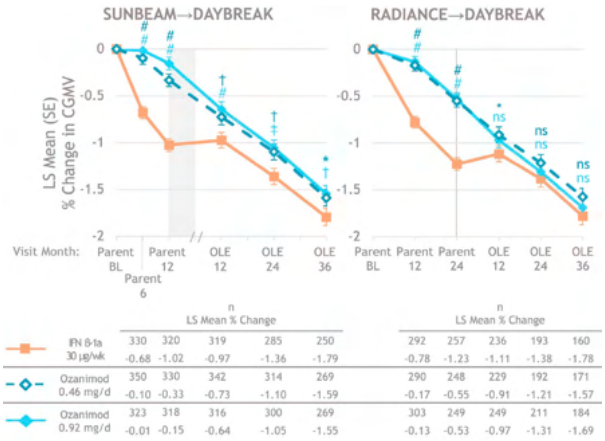

Figure 1 (B) CGMV

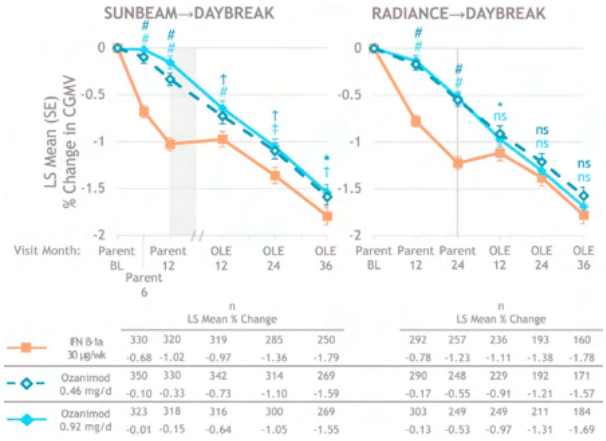

Figure 1 (C) TV

Conclusion: Switching from IFN to ozanimod reduced the rate of WBV, CGMV, and TV loss. Global and regional brain volume loss after 4–5 years of follow-up remained higher in participants who started on IFN than in continuous ozanimod users. These results support early treatment with ozanimod.

Disclosure: This study was supported by Bristol Myers Squibb, Princeton, NJ.

Sunday, June 20 2021
Movement Disorders: Biomarkers and Experimental

OPR-072

Functional connectivity as an early marker of indication for deep brain stimulation treatment in Parkinson's disease

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Background and aims: To identify early neuroimaging biomarkers for deep brain stimulation (DBS) in patients with Parkinson's disease (PD).
Methods: A cohort of PD patients prospectively recruited underwent clinical and cognitive evaluations and resting-state functional MRI (RS-fMRI) at baseline and every year for a maximum of four years. Patients were divided into two groups: 19 patients eligible for DBS (PD-DBS) over the 48-month follow-up and 41 patients who did not meet the criteria to undergo DBS surgery (PD-noDBS). Sixty age- and sex-matched controls performed baseline assessments. Graph analysis and connectomics assessed global and local topological network properties and regional functional connectivity (FC) at baseline and at time intervals.
Results: Lobar network analysis showed a significantly higher mean nodal strength, local efficiency and clustering coefficient of the occipital areas in PD-DBS relative to both controls and PD-noDBS at baseline. These results were then confirmed by regional analysis. A significantly decreased FC between sensorimotor/frontal and basal ganglia networks was found in PD-DBS compared to PD-noDBS patients at baseline. Referring to longitudinal analysis, PD-DBS patients showed a progressive decreased FC within occipital networks compared to PD-noDBS (stable over time). Progressively, increased FC between sensorimotor/frontal and basal ganglia networks occurred in PD-DBS compared to PD-noDBS (stable over time). At correlation analysis, FC within the occipital network were positively related to tremor in PD-DBS patients at baseline and over time.
Conclusion: RS-fMRI analysis might represent an early biomarker to help clinicians to establish the indication for DBS in PD patients.
Disclosure: Ministry of Education and Science Republic of Serbia (Grant #175090).

OPR-074

New Investigational DBS Lead and Burr Hole Device Improves Stability in Sheep Model

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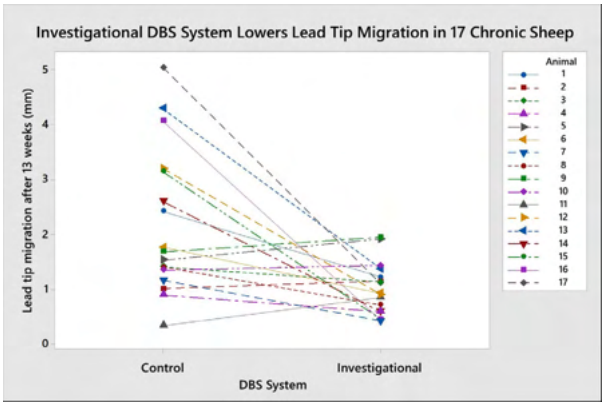
Background and aims: A market-released DBS lead and burr hole device (BHD, together the "control" system) has traditionally stabilized DBS leads with ring electrodes. Since newer segmented electrodes cluster at the center of the array and offer more programmability, improved chronic stability may ensure segmented electrodes remain near the stimulation target. A sheep study with a new DBS system ("investigational" and not commercially approved) tested the hypothesis that design changes improved lead stability compared to control.
Methods: 17 sheep were implanted contralaterally with control and investigational DBS systems. Implant and termination CT scans were segmented, processed, and registered. Distal electrode displacements were measured to assess chronic lead migration. A one-way analysis of variance assessed stability differences between the two systems and a line plot illustrated lead migration differences.
Results: Implant durations were 13.4±2.1 (SD) weeks. DBS lead tip displacements were 2.2±1.3mm for the control system and 1.0±0.5mm for the investigational system (p=0.002). As own in the line plot, a majority of leads experienced large differences in tip displacement while several differences were slight, suggesting that lead stability differences in some animals were too small to be reliably measured with CT scans.



Conclusion: The investigational DBS system demonstrated a statistically significant 55% improvement in chronic lead tip stability compared to the control DBS system in 17 sheep. These results suggest that design changes incorporated into the investigational DBS system can further stabilize the lead tip, potentially leading to better programmability and therapy optimization.
Disclosure: Walt Baxter, Ph.D.: Medtronic PLC: salary/employee/shareholder, Kelly Salb, M.S.: Medtronic PLC: salary/employee/shareholder.

OPR-076

Competing endogenous RNA networks and circular RNAs in peripheral blood cells of patients with Parkinson's disease

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Background and aims: New noninvasive and affordable molecular approaches that will complement current practices and increase the accuracy of PD diagnosis are urgently needed. CircRNAs are highly stable non-coding RNAs that accumulate with aging in neurons and are increasingly shown to regulate all aspects of neuronal development and function.he aims of the present study were to identify differentially expressed circular RNAs in peripheral blood mononuclear cells (PBMCs) of idiopathic PD patients and explore the competing endogenous RNA networks affected.

Methods: 87 circRNAs were initially selected based on relatively high gene expression in the human brain. Over half of these were readily detectable in PBMCsusing RT-qPCR. Comparative expression analysis was then performed in PBMCs from sixty controls and 60 idiopathic subjects with PD.

Results: Six circRNAs derived from MAPK9, HOMER1, SLAIN1, DOP1B, REPS1, and PSEN1 transcripts were significantly downregulated in PD patients. The classifier that best distinguished PD consisted of four circRNAs with an AUC of 0.84. Cross-linking immunoprecipitation-sequencing data revealed that the RNA-binding proteins bound by most of the deregulated circular RNAs include the neurodegeneration-associated FUS, TDP43, FMR1 and ATXN2. MicroRNAs predicted to be sequestered by most deregulated circular RNAs have the gene ontology categories 'protein modification' and 'transcription factor activity' mostly enriched.

Conclusion: This is the first study that identifies specific circular RNAs that may serve as diagnostic biomarkers for PD. Since they are highly expressed in the brain and are derived from genes with essential brain functions, they may also hint on the PD pathways affected.

Disclosure: Nothing to disclose.

OPR-090

The in-vivo diagnosis of synucleinopathies: a comparative study of skin biopsy and RT-QuIC

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Background and aims: The in-vivo diagnosis of synucleinopathies is particularly challenging. The aim of this study is to determine whether: 1) the immunofluorescence (IF) is a reproducible technique in detecting misfolded -synuclein (-syn) in skin nerves; and subsequently 2) IF and RT-QuIC (both in skin and CSF) show a comparable in-vivo diagnostic accuracy in distinguish synucleinopathies (SOPs) from non-synucleinopathies (non-SOPs) in a large cohort of patients

Methods: We prospectively recruited 90 patients fulfilling clinical and instrumental diagnostic criteria for all SOPs variants and non-SOPs (mainly including Alzheimer´s disease, tauopathies, and vascular parkinsonism or dementia). 24 patients with mainly peripheral neuropathies were used as controls. Patients underwent skin biopsy for IF and RT-QuIC whereas CSF was performed in patients who underwent lumbar puncture for diagnostic purposes. IF and RT-QuIC analysis were made blinded to the clinical diagnosis

Results: IF showed reproducible results between two pairs of neighbouring skin samples. Furthermore, both IF and RT-QuIC showed high sensitivity and specificity in discriminating SOPs from non-SOPs and controls but IF presented the highest diagnostic accuracy. IF presented a good level of agreement with RT-QuIC both skin and CSF in SOPs

Conclusion: 1) Both IF and RT-QuIC showed a high diagnostic accuracy although IF displayed the better value as well as an optimal reproducibility; 2) they presented a good level of agreement in SOPs supporting the use of a less invasive tests such as skin IF or RT-QuIC instead of CSF RT-QuIC as diagnostic tool for synucleinopathies

Disclosure: Nothing to disclose.

OPR-091

Optical coherence tomography: a potential biomarker of neurodegeneration in patients with Wilson's disease?

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Background and aims: WIlson's disease (WD) is an autosomal recessive disorder that leads to copper accumulation and deposition in different organs, frequently affecting visual pathways. Recent studies have detected morphological changes of retina in patients with WD using optical coherence tomography (OCT). The aim of this study was to evaluate the relationship between OCT parameters and form of the disease, therapy and symptoms duration, as well as severity of neurological impairment.
Methods: Study comprised 52 patients with WD and 52 healthy controls (HC). All the patients were on regular and stable chelation therapy and/or zinc salts. According to the main affected system, patients were divided in two groups, with neurological (NWD) or hepatic form of the disease (HWD). OCT was performed to assess the thickness of the RNFL (RNFLT).
Results: The intraocular pressure and the RNFLT were significantly lower in patients with WD when compared to HC. There were no differences between NWD and HWD in any of the ophthalmologically tested parameters. No significant correlations were found between clinical features and parameters of retinal thickness. The stratification of the cohort according to the disease duration showed that disease duration does not influence RFNL thickness.

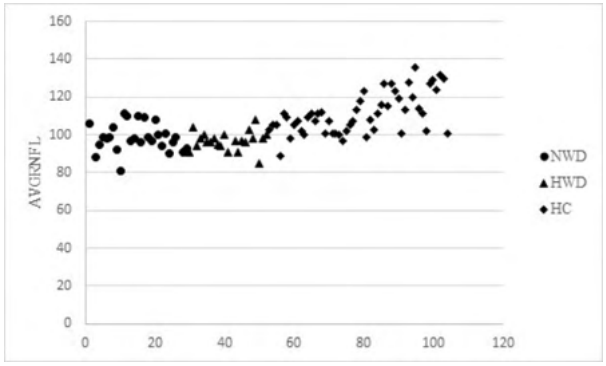

Figure 1. Values of average RNFL thickness in the superior and inferior segments in NWD and HWD patients and healthy control subjects

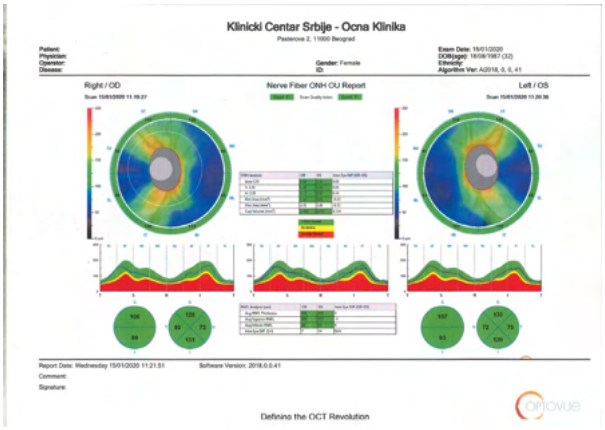

Figure 2: MS, right and left eye OCT, 32yrs, hepatic form

Conclusion: We found that involvement of retina represented subclinical finding in neurologically intact patients in HWD group. The value of the OCT as a biomarker for assessing clinical course and progression of WD still stays uncertain.
Disclosure: Nothing to disclose.

OPR-094

Characterising the role of alpha-synuclein in Ferroptosis in the context of Parkinson's disease

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Background and aims: Iron accumulation and intracellular inclusion of aggregated alpha synuclein (a-syn) are two main hallmarks in Parkinson's disease (PD). Iron deposition in the brain tightly correlates with a-syn deposition in the dorsal substantia nigra and cortex. Despite the involvement of alpha synuclein (a-syn) in Parkinson's disease (PD) pathology, the exact function of this protein and the mechanisms involved in the neuropathology remain unclear. Recently, we have shown that a novel regulated cell death pathway termed ferroptosis is predominant in pro-oxidant models of PD. Here we aim to demonstrate a pivotal interplay between a-syn, iron metabolism and ferroptosis in PD.

Methods: Via CRISPR/Cas 9 we have modulated endogenous a-syn and created stable human dopaminergic neuronal cell lines. Cell death in response to two different ferroptosis inducers was measured by resazurin assay. Levels of lipid peroxidation were equally assessed with C11-BODIPY by flow cytomery

Results: We observed that the absence of wild type a-syn conferred a protection against two ferroptosis inducers-Erastin and RSL3. This difference in cell viability was specific to ferroptosis since no difference was observed when inducing apoptosis or autophagic cell death. Levels of lipid peroxidation in response to Erastin or RSL3 were significantly less in the dopaminergic neurons lacking wild type asyn.

Conclusion: For several years, anti-apoptotic drugs have failed to afford any improvement in neuroprotection. For the first time, ferroptosis could represent the missing part to the puzzle in explaining the vicious circle between synucleinopathy, iron accumulation and subsequent cell death in Parkinson's disease.

Disclosure: The authors have nothing to declare.

Autonomic Nervous System Disorders

OPR-095

Heart-rate variability measured with wearable sensors is associated with disability status in multiple sclerosis

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Background and aims: New developments in sensor technology in recent years, facilitate novel approaches to assess neurological symptoms outside the clinic. Autonomic dysfunction is common in patients with multiple sclerosis (pwMS), but its role in the disease and its association with neurologic impairment is poorly understood. Therefore, we aim to assess the feasibility of studying heart rate variability (HRV), as a measure of autonomic dysfunction using wearable sensors and to correlate it with clinical measures of disease activity.
Methods: We studied 29 people with multiple sclerosis over the course of two weeks. Participants were continuously monitored with a wearable sensor. The data were subsequently cleaned and common HRV metrics were calculated and compared to the COMPASS-31 questionnaire.
Results: Of the calculated metrics most show a significant correlation with the COMPASS-31 and the EDSS. We compared the classification of the COMPASS-31 across the day. The best results are produced in the early morning hours by the normalized HF (AUC 0.84, CI: 0.69 to 0.99), normalized LF (AUC 0.84, CI: 0.69 to 0.99), pnn50 (AUC 0.78, CI: 0.61 to 0.95) and RMSSD (AUC 0.77, CI: 0.59 to 0.95).
Conclusion: Using a wearable to calculate HRV is feasible, reliable and poses a distinct advantage over standard ECG based methods. Our data suggests that early morning hours are the best time window to quantify autonomic dysfunction, when using a continuous measurement with a wearable sensor. Wearable sensors are a useful tool to assess and follow longitudinal changes in pwMS to study the impact of autonomic dysfunction in the disease.
Disclosure: No disclosures.

OPR-096

Cardiovascular autonomic neuropathy in type 2 diabetic patients

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Background and aims: Cardiovascular autonomic neuropathy is a common complication in type 2 diabetes mellitus (DM2) and is typically evaluated with measures of parasympathetic nerve fibre function. Few studies have assessed the sympathetic branch of the autonomic nervous system. Sympathetic neuropathy is associated with increased morbidity and mortality, and identification hereof is therefore imperative as conservative and/or pharmacological treatments are available. This study assessed sympathetic function in DM2 patients through standardized quantitative clinical testing.
Methods: 40 DM2 patients and 40 age- and gender-matched healthy controls (HC) were examined using Ewings autonomic test-battery, 24-hour blood pressure (24h-BP) profiling and self-reported COMPASS 31-questionaires.
Results: DM2 patients showed reduced parasympathetic activity with reduced inspiratory:expiratory-ratio (median [IQR] in DM2 1.11 [1.08-1–18] vs HC 1.18 [1.11–1.25] ($p=0.01$)) for deep breathing, and reduced heart rate variability measures in the time domain ($p<0.05$). No difference in cardiovascular sympathetic markers measured through the Valsalva manoeuvre was found ($p>0.05$) despite DM2 reporting more symptoms in the orthostatic domain of COMPASS-31 ($p=0.04$). 24h-BP showed reduced night-time systolic BP drop in DM2 (9.77%±8.84 vs. HC 15.72%±7.77 ($p<0.01$)) with an increased proportion of patients showing reverse dipping (9 DM2 vs. 1 HC $p=0.03$).
Conclusion: DM2 patients showed reduced parasympathetic activity, which is a known complication in DM2. No difference was found in short-term regulatory sympathetic markers, suggesting preserved cardiovascular sympathetic function. DM2 patients had altered circadian BP regulation, and reported more symptoms of orthostatic intolerance, indicating COMPASS-31 reported orthostatic intolerance and circadian BP regulation may not be sensitive markers of cardiovascular sympathetic neuronal dysfunction.
Disclosure: This research is supported by a Novo Nordisk Foundation Challenge programme grant (grant number NNF14OC0011633).

OPR-097

Orthostatic muscle excitability changes in neuropathic postural tachycardia syndrome

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Background and aims: The postural tachycardia syndrome (POTS) is a form of dysautonomia, characterized by chronic symptoms of orthostatic intolerance. 56–69% of patients report pain and muscle weakness in the lower extremities when upright, which is often accompanied by acrocyanosis. Muscle velocity recovery cycles (MVRCs) of muscle action potentials can be used to assess changes of muscle membrane potential. The present study examined muscle properties depending on body position in patients with neuropathic POTS and healthy controls.
Methods: In 10 patients and 10 control subjects repeated MVRCs of the left tibialis anterior muscle were recorded in the supine position and during 10 minutes of head-up tilt (HUT). Outcome measures included early supernormality, late supernormality and relative refractory period. Additionally, circumferences of the lower leg and experienced pain levels were assessed.
Results: Measurements of early supernormality and relative refractory period showed hyperpolarized muscle fibres in patients in the supine position, which depolarized faster during HUT compared to control subjects. Late supernormality revealed no significant changes. In parallel, the leg circumference increased during HUT significantly in patients only. Pain ratings were significantly higher in patients after five and 10 minutes of HUT.
Conclusion: The present results indicate postural changes in muscle membrane properties in patients with POTS. These alterations may be a consequence of inadequate perfusion of the muscles due to excessive pooling in the lower extremities.
Disclosure: The present study did not receive any funding and there are no conflicts of interest.

OPR-098

Compromised cardiovascular autonomic modulation in patient with acute ischemic stroke improves after three & six months

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Background and aims: Previous studies showed that patients with ischemic stroke have impaired cardiovascular autonomic modulation (CAM) with reduced parasympathetic and augmented sympathetic modulation. It is unclear whether CAM improves after several months. Therefore, we compared CAM of ischemic stroke patients in the acute phase, and three and six months after stroke.
Methods: In 82 ischemic stroke patients [33 women, 64.88±8.87 years], we recorded RR-intervals (RRI), systolic, diastolic blood-pressure (BPsys, BPdia), and respiration (RESP) at rest, during the first week, three and six months after stroke-onset. We calculated parameters reflecting total CAM [RRI-standard-deviation (RRI-SD), RRI-total-powers], sympathetic [RRI-low-frequency-powers (RRI-LF), BPsys-LF-powers] and parasympathetic CAM [Root-Mean-Square-of-Successive-RRI-Differences (RMSSD), RRI high-frequency powers (RRI-HF-powers)], and baroreflex-sensitivity (BRS). Patient-data were compared to data of 30 age-matched controls using repeated measurements of ANOVA Friedman-test with post-hoc analyses ($p<0.05$).
Results: In the first week, values of RRI, RRI-SD, RRI-total-powers, RRI-HF-powers, and BRS were significantly lower while BPsys-LF-powers were significantly higher in patients than controls. After three and six months, patients had significantly higher values of RRI, RRI-SD, RRI-total-powers, RMSSD, RRI-HF-powers, and BRS but lower values of BPsys-LF-powers than in the first week; RMSSDs and RRI-HF-powers no longer differed between patients and controls. However, after six months, RRIs, RRI-SD, and BRS were still lower in patients than controls.
Conclusion: In our patients, acute ischemic stroke caused cardiovascular autonomic dysregulation with decreased cardiovagal modulation and baroreflex sensitivity but increased sympathetic modulation. After three and six months, the initial autonomic impairment recovered but still showed minor autonomic imbalance with higher heart rates and lower baroreflex sensitivity.
Disclosure: The authors declare that there is nothing to disclose related to the study.

Child Neurology

OPR-099

Age at disease onset influences gray matter and white matter integrity in multiple sclerosis

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Background and aims: To investigate whether age at onset influences brain gray matter volume (GMV) and white matter (WM) microstructural abnormalities in adult multiple sclerosis (MS) patients, given its influence on clinical phenotype and disease course.
Methods: This hypothesis-driven cross-sectional study included 67 pediatric-onset MS (POMS) patients and 143 sex- and disease duration (DD)-matched randomly-selected adult-onset MS (AOMS) patients, together with 208 healthy controls. All subjects underwent neurological evaluation and 3T MRI acquisition. MRI variables were standardized based on healthy controls, to remove effects of age and sex. Associations with DD in POMS and AOMS patients were studied with linear models. Time to reach clinical and MRI milestones was assessed with product-limit approach.
Results: At DD=1 year, GMV and WM fractional anisotropy (FA) were abnormal in AOMS but not in POMS patients. Significant interaction of age at onset (POMS vs AOMS) into the association with DD was found for GMV and WM FA. The crossing point of regression lines in POMS and AOMS patients was at 19 years of DD for GMV and 15 for WM FA. For POMS and AOMS patients, median DD was 29 and 19 years to reach Expanded Disability Status Scale=3 ($p<0.001$), 31 and 26 years to reach abnormal Paced Auditory Serial Addition Task-3 ($p=0.01$), 24 and 19 years to reach abnormal GMV ($p=0.04$), and 19 and 17 years to reach abnormal WM FA ($p=0.31$).
Conclusion: Younger patients are initially resilient to MS-related damage. Then, compensatory mechanisms start failing with loss of WM integrity, followed by GM atrophy and finally disability.
Disclosure: Partially supported by grants from Italian Ministry of Health (GR-2009-1529671) and Fondazione Italiana Sclerosi Multipla (FISM2016/R/23).

OPR-100

Outcomes in 51 patients with cerebral ALD from two studies of elivaldogene autotemcel (eli-cel; Lenti-D) gene therapy

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Background and aims: Elivaldogene autotemcel (eli-cel; Lenti-D) gene therapy is being investigated in patients with cerebral adrenoleukodystrophy (CALD) in two open-label studies: ALD-102 and ALD-104.
Methods: Post-myeloablation, boys with CALD (≤17 years) received eli-cel (autologous CD34+ cells transduced with Lenti-D lentiviral vector encoding ABCD1 cDNA). After initial 2-year follow-up in ALD-102/ALD-104, monitoring will continue for 13 years in LTF-304. Data are median (minmax) as of October 2020 (ALD-102/ALD-104) and November 2020 (LTF-304).
Results: In ALD-102/LTF-304 (N=32), follow-up was 38.6 (13.4–82.7) months. The primary endpoint of major functional disabilities (MFDs)-free survival at Month 24 was met in 27/30 (90%) evaluable patients; two withdrew and one died after rapid disease progression. Of 28 patients still in ALD-102/LTF-304, none had MFDs through follow-up. Figure 1 shows neurologic function scores and Loes scores over time. At last visit, gadolinium enhancement resolved in 25/28 patients. Given limited follow-up in ALD-104 (N=19), only safety data as of 8.6 (0.1–16.8) months

are included. The safety/tolerability profile of treatment regimen in both studies primarily reflected known effects of mobilization/aphaeresis and myeloablation. Eli-cel-related adverse events included BK viral cystitis (n=1, SAE) and vomiting (n=2) in ALD-102, and pancytopenia (n=2, SAEs) in ALD-104. One ALD-104 patient experienced a transverse myelitis SAE (aetiology unknown), with ongoing ambulation issues and incontinence post-steroids/plasmapheresis. There was no graft failure, graft-versus-host disease, replication-competent lentivirus, or insertional oncogenesis.

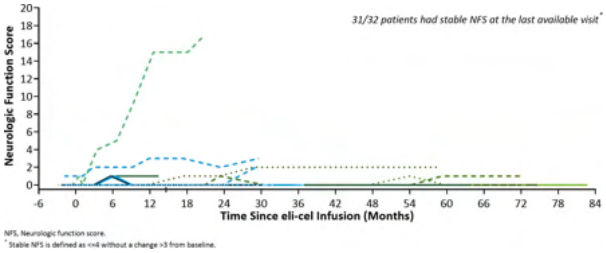

Figure 1A. Neurologic Function Score Over Time in ALD-102/LTF-304

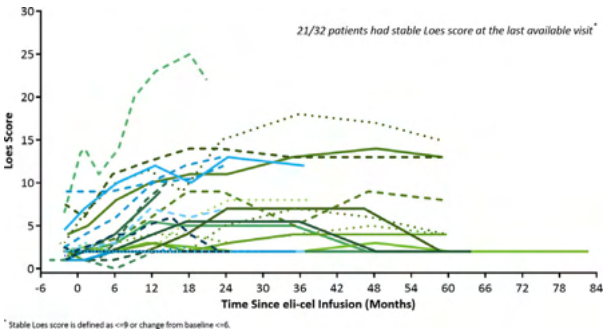

Figure 1B. Loes Score Over Time in ALD-102/LTF-304

Conclusion: As of October 2020, 51 eli-cel-treated patients were followed for up to 83 months with favourable safety profile. Neurologic function stabilised in ALD-102/LTF-304 and continues to be evaluated in ALD-104.
Disclosure: Sevin, Caroline: Consultant (bluebird bio, Inc.)

OPR-101

Association of prenatal exposure to antidepressants with standardized tests scores among Danish school-aged children

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Background and aims: This study evaluates whether prenatal exposure to antidepressants is associated with standardized test scores in Danish School Children.
Methods: Population-based cohort study of children born in Denmark between January 1, 1997 and December 31, 2009 who participated in the Danish National Test Program for public schoolchildren attending grades 2, 3, 4, 6, and 8 between January 1, 2010 and December 31, 2018 (n= 575,369 children with 2,178,923 test results). Primary outcomes were pooled test scores in mathematics and language. Test scores ranged from 1–100. Linear regression models with robust standard errors were used to estimate the difference in mean test scores between the exposure groups, while adjusting for potential confounders.
Results: Among the 575,369 children included in this study, 10,198 (1.77%) children were prenatally exposed to antidepressants. The overall mean score in mathematics and language was 56.79 (SD 24.44) and the mean score in mathematics was 57.26 (SD 25.02) and in language 56.53 (SD 24.11). When compared to unexposed children, prenatal exposure to antidepressants was associated with worse performance in the pooled score (difference: -0.90 (95% CI: -1.34; -0.45). The difference could only be observed in mathematics (-2.17, 95% CI: -2.71 to -1.63) but not in language (-0.16, 95% CI: -0.62 to 0.31).
Conclusion: Maternal use of antidepressants in pregnancy was associated with worse performance in mathematics but not in language tests among Danish school-aged children. The findings raise concern about potential long-term neurodevelopmental consequences of prenatal exposure to antidepressants.
Disclosure: Jakob Christensen received honoraria from serving on the scientific advisory board of UCB Nordic and Eisai AB, received honoraria from giving lectures from UCB Nordic and Eisai AB, and received funding for a trip from UCB Nordic.

OPR-102

Epilepsy and Psychiatric Disorders in Children with Congenital Disorders in the Danish Neonatal Screening Program.

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Background and aims: This study describes the long-term outcome of children with phenylketonuria (PKU) and congenital primary hypothyroidism (CH) – the two most frequent disorders included in the Danish Neonatal Screening Program.
Methods: We identified all children born in Denmark between 1 May 1981 and 31 December 2016 (n=2,218,308). We used the Danish National Hospital Register and the Psychiatric Central Research Register to identify children hospitalised with epilepsy and psychiatric disorders by 31 December 2016. Hazard ratios (HR) and corresponding 95% confidence intervals (95% CIs) were estimated using Cox Proportional Hazard Models adjusted for sex and calendar year.
Results: Among the overall study population, we identified 129 children with PKU (median age at diagnosis 0.4 years, males 51.2%) and 1,039 with CH (median age at diagnosis 14 days, males 35.7%). Among children diagnosed with PKU, 19 (14.7%) developed psychiatric disorders, and six (4.7%) developed epilepsy. Among children diagnosed with CH, 151 (14.5%) developed psychiatric disorders, and 39 (3.8%) developed epilepsy. Compared to children without PKU and CH, the risk of psychiatric disorders in children with PKU was HR=1.71 (95% CI: 1.09–2.68), and the risk of epilepsy was 3.46 (95% CI: 1.55–7.70). Compared to children without PKU and CH, the risk of psychiatric disorders in children with CH was 1.50 (95% CI: 1.28–1.76), and the risk of the risk of epilepsy was 2.56 (95% CI: 1.86–3.52).
Conclusion: The two major diseases included in the Danish Neonatal Screening Program (PKU and CM) were associated with increased risks of psychiatric disorders and epilepsy.
Disclosure: Funding: This work was supported by the National Institute of Neurological Disorders and Stroke (1R01NS106104-01A1), the Novo Nordisk Foundation (NNF16OC0019126), Central Denmark Region, and the Danish Epilepsy Association.

Movement Disorders: Treatment

OPR-078

Neurological manifestations of Wilson disease in treatment-naive patients and in patients receiving standard of care

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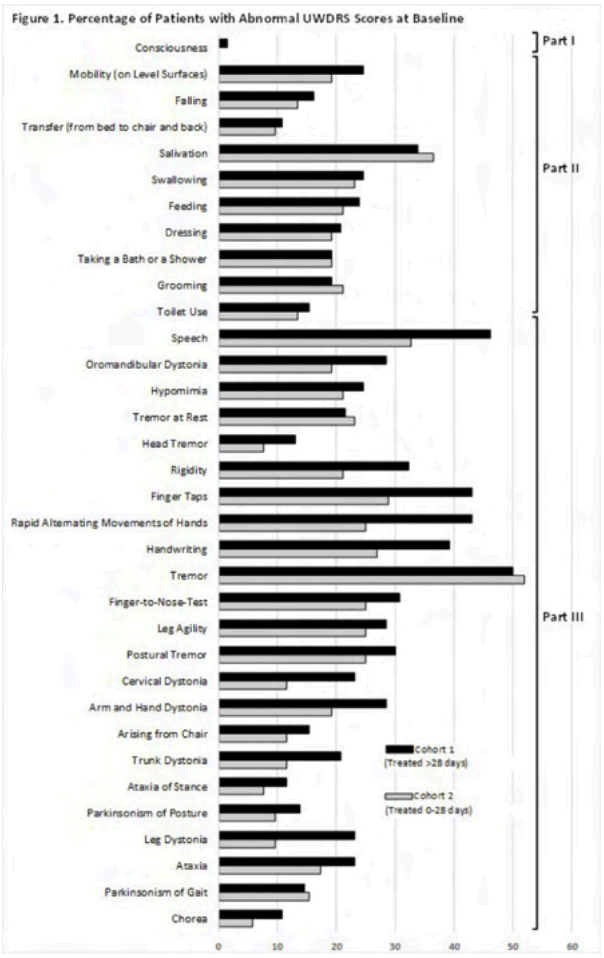
Background and aims: There is a lack of large cohort datasets presenting the neurological patients with Wilson disease (WD). An ongoing phase 3 study (NCT03403205) will assess the efficacy and safety of ALXN1840, a novel copper-binding agent in patients with WD. This interim analysis focuses on baseline neurological signs and symptoms of WD in this study.
Methods: The study includes two patient cohorts: Cohort 1; chronically treated patients who had previously received standard of care (SoC) for >28 days, Cohort 2; treatment naïve patients who could have previously received SoC from 0 to 28 days, prior to study enrollment. Eligible patients were 12 years of age with a diagnosis of WD confirmed by a Leipzig-Score 4. Patients could have a hepatic, extra-hepatic and/or neurologic phenotype. Neurological disease parameters were assessed at baseline using the Unified Wilson Disease Rating Scale (UWDRS) Part I (level of consciousness), II (disability) and III (neurologic examination) and were analyzed using descriptive statistics.
Results: 182 patients were enrolled between March 9, 2018 and January 30, 2020. Baseline UWDRS Part II, Part III and total score are shown by cohort and overall [Table 1]. Figure 1 shows the percentage of patients with abnormal UWDRS scores at baseline (i.e. a score >0). The most common neurological manifestations in Cohort 1 were tremors, impaired speech, finger taps and dysdiadokinesia and in Cohort 2 were tremor, salivation and impaired speech.

Table 1. UWDRS score at baseline

	Cohort 1 (Treated >28 days) N = 130	Cohort 2 (Treated 0-28 days) N = 52	All Patients N = 182
UWDRS Part II			
n	128	48	176
Mean (SD)	3.88 (7.342)	3.88 (7.019)	3.88 (7.235)
Median (IQR)	0.00 (3.00)	0.00 (4.00)	0.00 (3.00)
Q1, Q3	0.00, 3.00	0.00, 4.00	0.00, 3.00
Min, Max	0.0, 36.0	0.0, 25.0	0.0, 36.0
Patients with score >0, n	60	22	82
UWDRS Part III			
n	127	47	174
Mean (SD)	15.81 (20.293)	12.79 (18.158)	15.00 (19.733)
Median (IQR)	8.00 (20.00)	4.00 (18.00)	6.50 (19.00)
Q1, Q3	1.00, 21.00	1.00, 19.00	1.00, 20.00
Min, Max	0.0, 91.0	0.0, 71.0	0.0, 91.0
Patients with score >0, n	101	36	137
UWDRS Total Score			
n	125	47	172
Mean (SD)	19.93 (26.766)	16.79 (24.418)	19.07 (26.112)
Median (IQR)	9.00 (27.00)	5.00 (24.00)	8.00 (27.00)
Q1, Q3	1.00, 28.00	1.00, 25.00	1.00, 28.00
Min, Max	0.0, 127.0	0.0, 88.0	0.0, 127.0
Patients with score >0, n	100	37	137

Baseline is defined as last non-missing value on or before first study drug administration. SD = standard deviation; IQR = interquartile range; Q1, Q3 = 1st and 3rd quartile. UWDRS Part II, is patient/caregiver-rated and can range from 0 to 40 and Part III is clinician rated and can range from 0 to 175. Higher scores indicate worse disease rating. 'n' represents number of patients with non-missing values



Conclusion: Tremor and speech disturbances are the most common neurological symptoms in patients with WD in these cohorts.

Disclosure: AP, PH, DB, JB, DN, AC: investigators to Alexion Pharmaceuticals: AP, PH, AC: adviser to Alexion. AP: advisor to Vivet Therapeutics, Univar BV and GMP-Orphan Ltd. DB: adviser to Ultragenyx. CL: Alexion employee. DB: adviser to Ultragenyx.

OPR-089

Sialorrhea in advanced Parkinson's disease is associated to speech and swallowing disturbances

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Background and aims: Sialorrhea is an under recognised non-motor symptom of Parkinson's disease (PD) which has been associated to facial hypomimia. Aim of this study was to investigate whether sialorrhea in advanced PD might be related to speech and swallowing dysfunction and more severe motor and non-motor signs.

Methods: We collected the following demographic and clinical data from consecutive advanced PD patients: gender, age, age at onset, disease duration, total levodopa equivalent daily dose (LEDD) and LEDD dopamine agonists (D-Ag), Unified Parkinson's disease Rating Scale (UPDRS), Non-Motor Symptoms Scale (NMSS), SCOPA-autonomic questionnaire (SCOPA-AUT) and Parkinson's disease questionnaire-39 items (PDQ-39). Orofacial symptoms were measured using the Radboud Oral Motor Inventory for PD (ROMP), a self-administered questionnaire evaluating speech, swallowing disturbances, and drooling of saliva. PD with and without sialorrhea (PD-droolers, PD-non-droolers) were compared for all variables. We defined PD-droolers those scoring >1 at UPDRS-II item 6.

Results: We included 101 PD patients, of which sixty-five (64.4%) were classified as PD-"droolers" and 36 (35.6%) as PD-"non-droolers". UPDRS-III was more severe in the OFF ($p=0.03$) and ON medication state ($p=0.002$) in PD-droolers, who also had lesser improvement at the levodopa challenge test ($p=0.007$). At ROMP, PD-droolers had more severe speech ($p<0.0001$) and swallowing ($p<0.05$) dysfunction. NMSS ($p=0.0008$) and SCOPA-AUT ($p=0.003$) scored higher in PD-droolers. Quality of life by PDQ-39 ($p=0.049$) was poorer in PD-droolers.

Conclusion: Sialorrhea in PD is associated to more severe motor and non-motor symptoms, speech and swallowing dysfunction and significant burden of non-motor and autonomic symptoms.

Disclosure: No disclosures.

OPR-106

Quantifying the incremental economic burden of Advanced Parkinson's disease: Real-world Evidence from EU5 countries

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Background and aims: Parkinson's disease (PD) is among world's fastest growing neurodegenerative disorders. Recent efforts to quantify the burden of PD have identified the need for further understanding of the incremental economic burden in higher disease severity.

Methods: We conducted a cross-sectional analysis of the Adelphi Parkinson's disease Specific Programme™ (2017–2019). The study evaluated real-world Persons with PD (PwP) receiving care in EU5 (Spain, Italy, UK, France, Germany). Patients were grouped according to physician judgement of PD severity (early, intermediate, advanced). The economic burden was measured based on annual healthcare resource utilization (HCRU) including direct medical and indirect costs. Annual costs were based on 2017-2018 UK reference and converted to Euros using 2020 currency rate. Binary and generalized linear models were computed to estimate costs across disease severity (adjusted for country, age, sex, and Charlson comorbidity index).

Results: We included 3,486 PwP (Age: 69.4±10.4 years; Time since diagnosis: 5.1±5.1 years) with 18% classified as advanced PD. Compared to early PD, Advanced PD patients were considerably more likely to utilize comprehensive care such as professional care (29.9x higher), non-professional care (18.6x higher), and hospitalizations (14.4x higher) [Table 1]. Overall annual mean HCRU costs increased significantly with advancing PD severity (Early: €2,110, intermediate: €11,431, Advanced: €38,625) [Table 2]. Key drivers for high annual HCRU costs among advanced PD patients included professional care (€20,300), respite care (€ 11,972), and hospitalizations (€ 3,225).

12-Month Healthcare Resource Utilization	Intermediate PD (n=1433)		Advanced PD (n=631)	
	OR [a]	(95% CI) [a]	OR [a]	(95% CI) [a]
Overall Utilization	1.34	(0.93, 1.94)	1.35	(0.79, 2.30)
Hospitalizations	5.02	(3.62, 6.95)	14.43	(10.11, 20.61)
Emergency Room Visits	3.08	(2.21, 4.29)	5.83	(4.07, 8.37)
Consultations [b]	1.45	(1.10, 1.91)	0.95	(0.67, 1.35)
Scans [c]	0.65	(0.55, 0.76)	0.50	(0.40, 0.63)
Professional care [d]	7.31	(4.23, 12.63)	29.91	(17.26, 51.84)
Respite care	5.21	(3.30, 8.21)	14.98	(9.33, 24.05)
Non-professional Care [e]	6.12	(3.31, 11.30	18.63	(9.80, 35.42)

Abbreviations: OR: Odds ratio; CI: Confidence Interval. **Notes**: a: Logistic regression model estimating odds of any utilization with Early PD as reference and adjusted for country, patients age, sex, and Charlson comorbidity index; b: Consultations include visits to any of the following: GP/PCP, consultant, and/or PD nurse; c: Scans include any of the following: MRI, CT, SPECT, fMRI, DaT, and/or PET; d: Professional care include any of the following: district nurse, nursing home staff, home help, psychiatric nurse, physiotherapist, speech therapist, social worker, and/or other; e: Non-professional care is based on reduction in weekly working hours due to caregiving as incurred by non-professional caregivers (i.e. spouse, adult son/daughter, other relative, friend, other).

Table 1: Annual healthcare resource utilization of patients with Parkinson's disease

12-Month Healthcare Costs	Early PD (n=1422)		Intermediate PD (n=1433)		Advanced PD (n=631)	
	Mean [a]	(95% CI) [a]	Mean [a]	(95% CI) [a]	Mean [a]	(95% CI) [a]
Overall Costs (Euro) [b]	2110	(1014, 4843)	11431	(6327, 20567)	38625	(23797, 61935)
Hospitalizations	184	(97, 340)	1057	(693, 1580)	3225	(2247, 4529)
Emergency Room Visits	9	(5, 15)	36	(23, 53)	95	(65, 136)
Consultations [c]	270	(233, 311)	350	(304, 399)	471	(393, 557)
Scans [d]	239	(185, 308)	149	(111, 198)	105	(72, 149)
Professional care [e]	317	(102, 936)	4130	(2312, 7227)	20300	(13009, 31223)
Respite care	872	(311, 2376)	4774	(2396, 9370)	11972	(6676, 21018)
Non-Professional Care [f]	220	(82, 557)	936	(487, 1738)	2458	(1335, 4323)

Abbreviations: CI: Confidence Interval. **Notes**: a: Two-part regression model including probit and generalized linear models (inverse Gaussian with log link function) estimating predicted mean costs and adjusted for patients country, age, sex, and Charlson comorbidity index; b: Unit costs are based on 2017-2018 UK reference costs and were converted to euros based on 2020 currency exchange rate (1 GBP=1.1237 EUR); c: Consultations include visits to any of the following: GP/PCP, consultant, and/or PD nurse; d: Scans include any of the following: MRI, CT, SPECT, fMRI, DaT, and/or PET; e: Professional care include any of the following: district nurse, nursing home staff, home help, psychiatric nurse, physiotherapist, speech therapist, social worker, and/or other; f: Non-professional care is based on reduction in weekly working hours due to caregiving as incurred by non-professional caregivers (i.e. spouse, adult son/daughter, other relative, friend, other).

Table 2: Annual healthcare costs of patients with Parkinson's disease

Conclusion: PwP experience substantial and incrementally higher economic burden with advancing PD. Future intervention to alleviate PD symptom burden and delay progression may reduce future economic burden.

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OPR-145

Falls Predict Acute Hospitalization in Parkinson´s Disease

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Background and aims: The aim of the present study was to identify predictors of acute unplanned hospitalization in Parkinson´s disease (PD).

Methods: PD patients recruited from 35 centers of Spain from the COPPADIS cohort from January 2016, to November 2017, were included in the study. Patient baseline evaluation included motor assessment, non-motor symptoms (NMS), cognition, mood and neuropsychiatric symptoms, disability, and quality of life. Kaplan-Meier estimates were obtained and Cox regression performed on time to hospital encounter 1-year after the baseline visit.

Results: Thirty-five out of 605 (5.8%) PD patients (62.5 ± 8.9 years old; 59.8% males) presented an acute unplanned hospitalization during the 1-year follow-up after the baseline visit. Traumatic falls (9 events) represented the most frequent cause of admission, being 56.3% of all indirect PD-related morbidity causes and 23.7% and 18.4% of all acute unplanned (38 events) and all hospitalizations (49 events), respectively. To suffer from motor fluctuations (HR [hazard ratio] 2.461; 95% CI, 1.065–5.678; p=0.035), a very severe NMS burden (HR [hazard ratio] 2.828; 95% CI, 1.319–6.063; p=0.008), falls (HR 3.966; 95% CI 1.757–8.470; p=0.001), and dysphagia (HR 2.356; 95% CI 1.124–4.941; p=0.023) was associated with acute hospitalization after adjustment to age, gender, disease duration, levodopa equivalent daily dose, total number of non-antiparkinsonian drugs, and UPDRS-III-OFF. Of the previous variables, only falls (HR 2.998; 95% CI 1.080–8.322; p=0.035) was an independent predictor of acute hospitalization.

Conclusion: Falls is an independent predictor of acute unplanned hospitalization in PD patients.

Disclosure: Nothing to disclose.

OPR-147

Clinical and imaging features of idiopathic cerebellar ataxia with anti-cerebellar antibodies

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Background and aims: Idiopathic cerebellar ataxia (IDCA) is the clinical-based term for sporadic cerebellar ataxia with insidious onset and a slowly progressive course. Despite a heterogeneous pathogenesis, diagnostic criteria for IDCA were recently proposed on the basis of those for sporadic adult-onset cerebellar ataxia of unknown etiology, albeit with slight modifications. The purpose of this study was to determine whether autoimmunity can account for some cases of IDCA.
Methods: Using tissue-based immunofluorescence assay (TBA), we examined the expression of anti-cerebellar antibodies (ACAs) in serum samples from 47 patients who met the IDCA diagnostic criteria and control subjects, including 20 patients with multiple system atrophy (MSA), 13 with hereditary ataxia (HA), and 17 healthy subjects. Clinical and imaging features were compared between ACA-positive and ACA-negative IDCA patients.
Results: ACAs were detected in the serum samples of 34% patients with IDCA. This prevalence of ACAs was significantly higher than that of patients with MSA (10%, p=0.037), HA (0%, P = 0.010), or healthy subjects (6%, p=0.016). ACA-positive IDCA patients frequently showed asymmetrical cerebellar hypoperfusion on single-photon emission computed tomography (SPECT) and tended to show pure cerebellar ataxia. The progression of cerebellar ataxia in IDCA patients with neuropil staining of molecular layer is faster than that of patients with intracellular staining of Purkinje cell.
Conclusion: We detected ACAs in 34% of IDCA patients. Autoimmunity can account for some cases of IDCA. The characteristic clinical features of ACA-positive IDCA patients were asymmetrical cerebellar hypoperfusion on SPECT and pure cerebellar ataxia.
Disclosure: The authors declare that they have no competing interests.

OPR-148

Reliability and validity of passively measured gait, gestures from smartphones and smartwatches in Parkinson's disease

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Background and aims: Motor functioning in daily life is the most ecologically valid reflection of motor disease severity, but is difficult to quantify objectively. Smartphones and smartwatch sensors worn by patients enable the passive quantification of motor behavior in daily life, but it is unclear whether these metrics are reliable and clinically meaningful. Here we determined the reliability and clinical validity of such measures in individuals with early Parkinson's disease (PD).
Methods: Baseline PASADENA clinical trial (NCT03100149) data from 316 individuals with early PD were analyzed. Passive sensor features of gait and gestures were averaged over 14 days. Test-retest reliability was assessed by calculating intraclass correlation coefficients of sensor features over two consecutive fortnights. Spearman's rank order correlations tested for associations between sensor features and MDS-UPDRS scores.
Results: Test-retest reliabilities of passively monitored gait and gesture sensor feature were high (ICC's>0.7; p<0.001). Hand gesture features negatively correlated with MDS-UPDRS parts 1–3, bradykinesia and rigidity subscores (-0.37rs[df263]-0.17, p<0.05), and positively correlated with tremor subscores (0.17rs[df263]0.21, p<0.05). Gait measures negatively correlated with MDS-UPDRS parts 2, 3, bradykinesia, and postural stability subscores (-0.35rs[df264]-0.15, p<0.05), and positively with freezing of gait scores (rs[df264]=0.26, p<0.001). Regression analyses with MDS-UPDRS scores (outcomes) and sensor features (predictors) confirmed these results.
Conclusion: Gait and gestures in daily life, passively monitored with smartphones and smartwatches, were associated with physicians' ratings of motor symptom severity, even in this early population with overall mild symptom levels. These findings support the preliminary reliability and validity of passively monitored daily motor behavior with the Roche PD Mobile Application v2.
Disclosure: This research was funded by F. Hoffmann-La Roche AG and Prothena Biosciences Inc.

Multiple Sclerosis: MRI in MS and related disease

OPR-109

Clinical Relevance of Multiparametric MRI Assessment of Cerebellar Damage in Multiple Sclerosis

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Background and aims: To explore cerebellar damage in multiple sclerosis (MS) with multiparametric MRI, and to identify MRI predictors of physical disability and cognitive impairment.
Methods: 164 MS patients (89 relapsing-remitting [RR] and 75 progressive MS [PMS]), and 68 age- and sex-matched healthy controls underwent brain and cervical spinal cord (CSC) 3T MRI with pulse sequences for assessing lesions and atrophy in the brain (separately for cerebellum, brainstem and supratentorial areas) and CSC; and microstructural damage (with diffusion-tensor metrics) of the cerebellar peduncles. Subjects underwent neurological examination, and neuropsychological assessment with the Brief Repeatable Battery. Domain-specific z-scores were averaged yielding a cognitive z-score. MRI predictors of clinical variables were identified with random forest models.
Results: In RRMS patients, predictors of higher Expanded Disability Status Scale (EDSS) score were: higher brainstem, CSC GM and middle cerebellar peduncle lesion volumes (LV), and CSC atrophy (out-of-bag [OOB]-R2=0.35). In PMS patients, predictors of higher EDSS score were: CSC and cerebellum lobule I-IV GM atrophy, and longer disease duration (OOB-R2=0.16). In RRMS patients, predictors of lower cognition z-score were: thalamic and brain atrophy, cerebellum lobule IX and Crus2 GM atrophy, supratentorial and superior cerebellar peduncle LV (OOB-R2=0.18). In PMS patients, predictors of cognition z-score were: brain GM, thalamic and cerebellum Crus2 GM atrophy, supratentorial LV (OOB-R2=0.22).
Conclusion: Atrophy of specific anatomo-functional sub-regions of the cerebellum conveys important predictive information for physical disability and cognitive impairment in MS patients. Lesions in the cerebellar peduncles also play a relevant role, particularly in RRMS.
Disclosure: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

OPR-110

Relevance of NODDI to characterise microstructural abnormalities of MS cortex and cortical lesions in vivo: a 3T study

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Background and aims: Neurite orientation dispersion and density imaging (NODDI) could better evaluate multiple sclerosis (MS)-related damage to cortical microarchitecture. Using NODDI, we characterized the microstructural abnormalities of normal-appearing cortex (NA-cortex) and cortical lesions (CLs) and their relations with MS phenotypes and clinical disability.
Methods: One hundred and seventy-two patients with MS (PwMS) (101 relapsing-remitting [RR], 71 progressive [P]) and 62 healthy controls (HC) underwent a brain 3T acquisition. Brain cortex and CLs were segmented from 3D T1-weighted and double inversion recovery, respectively. Using NODDI on diffusion-weighted sequence, intracellular (ICV_f) and extracellular volume fractions (ECV_f) and orientation dispersion index (ODI) were assessed in NA-cortex and CLs.
Results: One hundred and seventeen (68.3%) PwMS had one CL. PwMS NA-cortex had a significant lower ICV_f vs HC NA-cortex (p=0.001). CLs showed a significant increased ECV_f (p<0.001) and decreased ICV_f and ODI vs NA-cortex of both HC and PwMS (p0.006). Compared to RRMS, PMS had a significant decreased NA-cortex ICV_f (p=0.03). Higher CL burdens were found in PMS vs RRMS (p<0.001), without microstructural differences. MS NA-cortex ICV_f, ECV_f and ODI were significantly correlated with disease duration, EDSS, white matter and CL burdens, and brain atrophy (r from -0.51 to 0.71, p from <0.001 to 0.02).
Conclusion: A significant neurite loss occurs in MS NA-cortex. CLs show a further neurite density reduction, an increased extracellular space, reflecting inflammation and gliosis, and a reduced ODI suggesting a simplification of neurite complexity. NODDI is relevant to investigate in vivo the heterogeneous pathology affecting MS cortex.
Disclosure: This study was supported by Fondazione Italiana Sclerosi Multipla with a senior research fellowship (FISM2019/BS/009) and a research grant from (FISM2018/R/16), and financed or co-financed with the '5 per mille' public funding.

OPR-111

Characterizing 1-year cervical cord atrophy progression in different MS phenotypes: a voxel-wise, multicenter analysis

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Background and aims: In multiple sclerosis (MS), the cervical spinal cord frequently shows irreversible tissue loss. Here, we evaluated voxel-wise distribution and changes over time of cervical cord atrophy in a MS dataset acquired at seven European sites.

Methods: Baseline and 1-year clinical and 3D T1-weighted cervical cord data were obtained from 54 healthy controls (HC) and 110 MS patients (13 clinically isolated syndrome [CIS], 75 relapsing-remitting [RR] and 22 progressive [P] MS). An optimized pipeline was used to assess voxel-wise differences of cervical cord atrophy, their longitudinal changes and correlations with clinical variables.

Results: MS patients exhibited significant ($p<0.05$, family-wise error [FWE] corrected) baseline cervical cord atrophy vs HC in C1/C2 anterior, posterior/lateral, and C4–C6 posterior cord. While CIS patients showed slight cord expansion vs HC at posterior C4, RRMS presented significant cord atrophy vs CIS at posterior/lateral C2–C4, and PMS showed widespread cord atrophy vs RRMS patients at C4–C5 and C7. During the follow-up, a significant cord atrophy progression ($p<0.05$, FWE) was detected in MS at posterior/lateral C2 and C4–C6. Such progression was driven by RRMS, while CIS did not show cord atrophy changes over time, and PMS patients showed circumscribed tissue loss at posterior C2-C6. Baseline clinical disability was strongly related ($p<0.05$, FWE) with baseline cord atrophy at posterior/lateral C2–C4. Also, baseline atrophy at lateral C3-C4 was able to explain clinical disability at 1-year follow-up.

Conclusion: Voxel-wise analysis of cervical atrophy characterized 1-year evolution of tissue loss across phenotypes. Cord atrophy was clinically relevant and contributed to explain follow-up disability.

Disclosure: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

OPR-112

Classifying and characterizing multiple sclerosis disease phenotypes with functional connectivity and machine learning

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Background and aims: Graph theoretical analysis is helping to shed light into brain functional reorganization in multiple sclerosis (MS). Here, we developed advanced machine-learning methods to analyse resting state (RS) functional connectivity (FC) data and classify MS patients according to their disease phenotype.
Methods: RS fMRI scans were obtained from 46 healthy controls (HC) and 113 MS patients (62 relapsing-remitting [RR]; 51 progressive [P]MS). Dominant sets clustering was used to group covariance-based RS FC matrices into clusters of subjects sharing some similarities in their network configuration. Support vector machines (SVMs) were then used to classify disease phenotypes exploiting a representation of networks based on their geodesic distance from cluster means. Finally, a sensitivity analysis on the trained classifier was used to identify clusters and connections more relevant for classification.
Results: The described machine-learning tool was able to classify RRMS patients from HC with an accuracy of 72.5%, PMS patients from HC with an accuracy of 84.1% and PMS from RRMS patients with an accuracy of 76%. The sensitivity analysis on trained SVMs found that increased connectivity within the basal ganglia sub-network and decreased RS FC within the temporal sub-network contributed to an accurate classification of both RRMS and PMS patients from HC. Moreover, decreased RS FC within the occipital and parietal sub-networks contributed to differentiate PMS patients from HC.
Conclusion: A combination of different machine learning principles allowed to classify MS patients with different clinical phenotypes from HC with a good accuracy. Distinct sub-networks abnormalities contributed to an accurate phenotype classification.
Disclosure: Partially supported from by a grant from Fondazione Italiana Sclerosi Multipla (FISM/2018/R/5) and financed or co-financed with the '5 per mille' public funding.

OPR-113

Choroid plexus enlargement characterizes inflammatory multiple sclerosis

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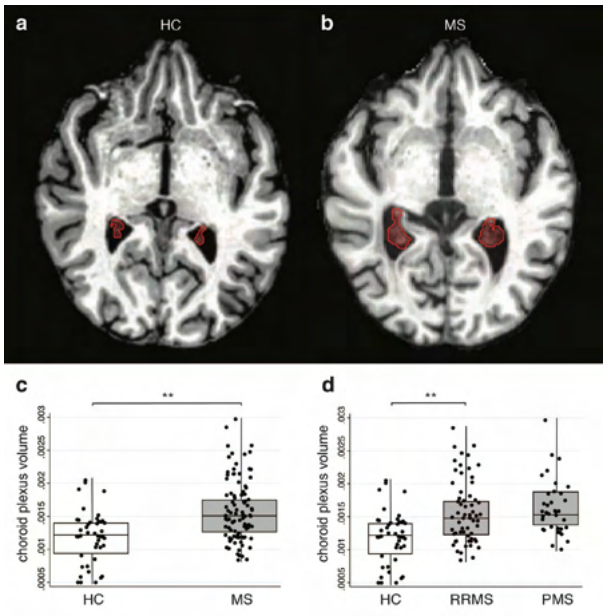
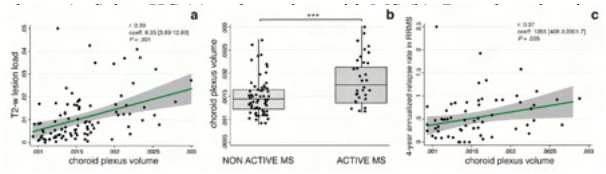
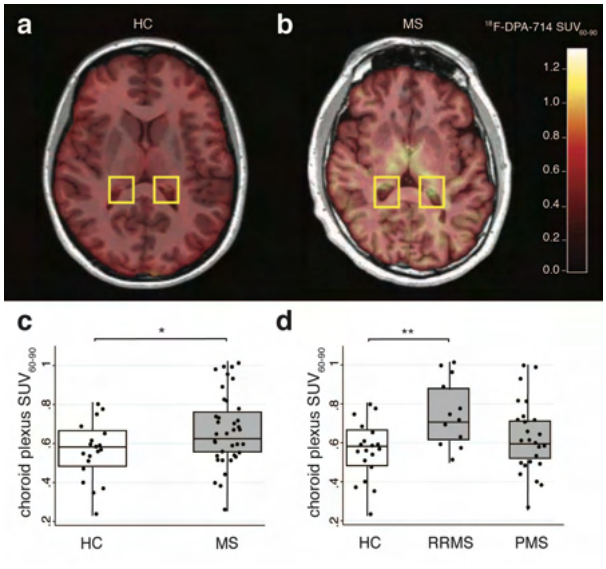
Background and aims: A role for choroid plexuses (CPs) was shown in experimental autoimmune encephalitis, but we lack in vivo evidence in patients with multiple sclerosis (MS).
Methods: 97 patients with MS (61 relapsing-remitting, RRMS, 36 progressive, PMS) and 44 healthy controls (HC) underwent 3T MRI; a subgroup of 37 patients and 19 HC underwent translocator protein (TSPO) 18F-DPA-714 PET to quantify neuroinflammation. Relapses and disability scores were collected at baseline and through a 2-year follow-up. CPs were manually segmented on 3DT1-weighted images. Whole brain, thalamus, normal-appearing white matter (NAWM), cortex, T2-hyperintense and gadolinium-enhancing lesions were additionally segmented. 18F-DPA-714 distribution volume ratio was quantified in parenchymal ROIs, whereas standardized uptake value was used to quantify inflammation in CPs. Multivariable linear regressions were fitted to assess: i) CP volumetric and inflammatory differences between patients and HC; ii) correlations between CP volume and lesion load, brain volumes, parenchymal inflammation and annualized relapse rate (ARR).
Results: CPs were 35% larger in MS compared to HC ($p=0.004$), particularly in RRMS ($p=0.008$, fig.1). CP enlargement was higher in patients with gadolinium-enhancing lesions ($p<.001$), and correlated with brain inflammation as reflected by WM lesion load ($r:0.39$; $p<0.001$), thalamic and NAWM 18F-DPA-714 binding ($r:0.44$; $p=0.04$, and $r:0.5$; $p=0.005$). Moreover, it correlated with ARR in RRMS ($r:0.37$;$p=.005$, fig.2). Finally, patients showed 17.5% higher CP 18F-DPA-714 uptake ($p=.016$, fig.3), which correlated with CP volume in RRMS ($r:0.58$; $p=0.01$).
Conclusion: CPs are enlarged and inflamed in MS, particularly in patients with RRMS with an inflammatory profile. CP volumetric analysis could represent a novel imaging marker in MS.
Disclosure: The authors declared no conflict of interest related to this work. V.A.G.R. reports fees for traveling from Novartis and Roche.



T1-w images showing the segmentation of the left and right choroid



Scatter plots of the association of higher choroid plexus volume with greater T2 lesion load in MS patients (a) and with 4-year annualized relapse rate in RRMS (c). Box plot showing that MS with at least one gadolinium+ lesion had larger CPs (b).



18F-DPA-714 standardized uptake value (SUV60-90) maps of a HAB HC (a) and a HAB patient with MS (b). Box plot showing greater CP inflammation, measured as 18F-DPA-714 SUV60-90, in the whole MS cohort vs HC (c), and in RRMS or PMS separately vs HC (d).

OPR-114

Leptomeningeal enhancement under anti-CD20 therapies – a monocentric retrospective cohort study of 70 patients

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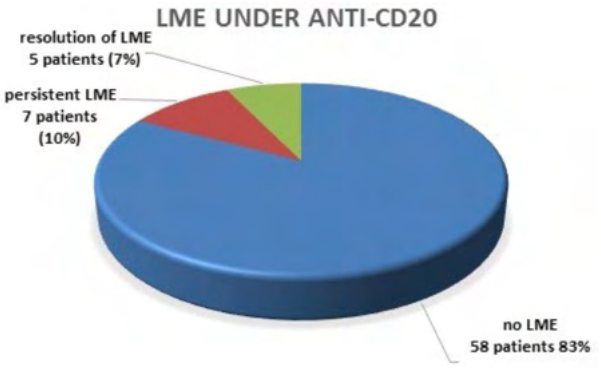
Background and aims: Evaluate the evolution of leptomeningeal enhancement (LME) as a new imaging biomarker of disease activity under treatment with anti-CD20 therapies.

Methods: Retrospective analysis of clinical and MRI data regarding LME of 70 multiple sclerosis (MS) patients treated with ocrelizumab or rituximab in a tertiary neurological center in Switzerland.

Results: We evaluated 70 MS patients (mean age 47 years, range 24–81 years, 39 female); 17 (24%) with primary progressive (PP) and 53 (76%) with relapsing remitting (RR) MS. 18 (26%) patients were initially treated with rituximab (later switched to ocrelizumab) and 52 (74%) initially with ocrelizumab. 18 patients (26%) had no treatment before anti-CD20 therapies. Each patient had one MRI exam before initiation and at least one (range 1–8) during treatment (mean 4.7 MRI exams per patient). Mean observed treatment duration was 18 months (range 1–80 months). Mean disease duration was 126 months (range 24–456 months). 58 patients (83%; 43 RRMS, 15 PPMS) had no LME, seven patients (10%; six RRMS, one PPMS) had persistent LME, whereas five patients (7%; four RRMS, one PPMS) showed resolution of LME under anti-CD20 therapy (all under ocrelizumab).



Conclusion: In our cohort of 70 patients, we detected resolution of LME in 7% of MS patients (both RR and PP) under treatment with anti-CD20 therapies, a finding that has not been described so far. As LME plays an important role in cerebral gray matter pathology, further investigations, correlation with clinical phenotypes and a comparison with other immunotherapies are needed.

Disclosure: No disclosures related to this manuscript.

Neurotraumatology

OPR-115

Automated pupillometry to uncover signs of consciousness in acute brain injury

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Background and aims: Cognitive and emotional processes evoke pupillary dilation and may act as surrogate marker for brain activity. Automated pupillometry has shown promising results in quantifying pupil motility and can easily be performed serially at the bedside at low-cost. As cognitive stimuli such as mental arithmetic or emotional stimuli generate pupil dilation, we hypothesize that automated pupillometry may have a role in assessment of consciousness in acute brain injuries if proven sensitive enough to detect responses to standardized stimuli.

Methods: We assess automated pupillometry in healthy volunteers, neurological patients suffering from acute brain injury and cardiac arrest patients in the ICU during and after sedation. Pupillary function is registered over time while subjects are shown their reflection in a mirror, hear auditive stimuli and are asked to perform mental arithmetic's.

Results: Pilot data have been collected on 22 healthy subjects (male 72%; median-age 62), as well as 29 patients with cardiac arrest (n=21) or other brain injury (n=8). 72% of healthy controls reacted with pupil dilation on two of the auditive stimuli, while only 18% responded to their own reflection. 10 subjects show at least 4/5 dilations in both difficulties of mental arithmetic's. Lowering the cut-off to a minimum of three dilations, the pilot data show respectively 64% (n=14) and 59% (n=13) succession rate, suggesting cognitive processing of mental tasks.

Table 1: Pilot data

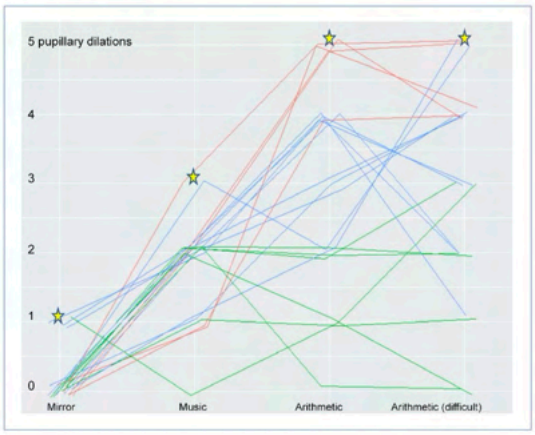
Dilations	Mirror (n=22)	Music (n=22)	MA Medium (n=22)	MA Hard (n=22)
0	18	1	2	1
1	4	5	2	3
2	-	14	4	5
3	-	2	4	3
4	-	-	6	6
5	-	-	4	4
Success rate	18%	72%	45%	45%

Abbreviations: MA=Mental arithmetic; n=number of subjects

Dilations for each patient

Figure 2

This figure depicts results from pupillary measurements in control subjects. Healthy volunteers (n=22) were asked to focus on their reflection in a mirror, listened to an audio tape with three short sequences of music intermixed with silence, and perform series of mental arithmetic with different degrees of complexity (x-axis). Automated pupillometry was used to assess pupillary dilation as evidence of arousal (mirror, music) and sustained attention/command following (arithmetic). The y-axis reveals the number of pupillary dilations for individual subjects during each of the four tests, and the stars denote the maximal number of possible dilations during each task (i.e. from 1 dilation for the mirror task to 5 dilations for arithmetic). Successful command following was defined by ≥4 significant pupillary dilations during five mental arithmetic tasks. Subjects who were able to follow commands and successfully engage in both arithmetic tasks, as evidenced by pupillary dilations, are shown in red (n=6). Subjects able to do so in one of the two arithmetic tasks are shown in blue (n=11). Those who did not pass the threshold of 4/5 dilations in neither of the two tasks, suggesting that they were unable to sustain attention, are depicted in green (n=7).



Conclusion: We suggest that automated pupillometry is worthy of further exploration in the assessment of consciousness following acute brain injuries. Applying this tool in the setting of ICU could help detect patients with covert consciousness.

Disclosure: Nothing to disclose..

OPR-116

Overexpression of miR-26a promotes neurite regeneration in the central nervous system in vitro

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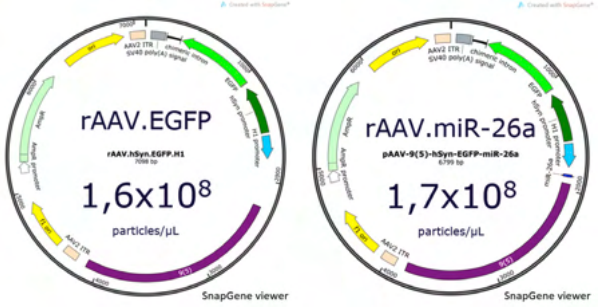
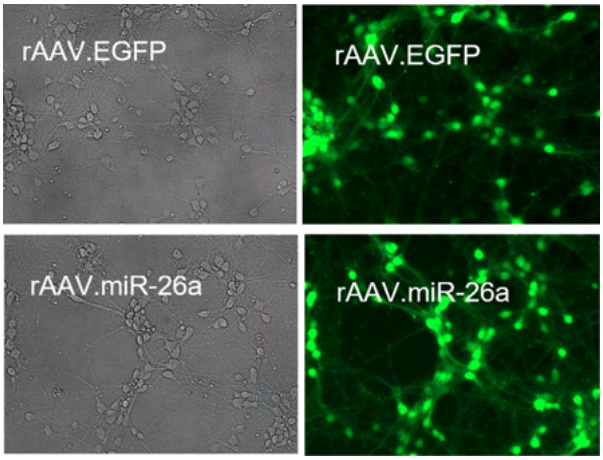
Background and aims: The central nervous system (CNS) has an intrinsic low capacity for axon regeneration due to an imbalance in gene expression. Thus, investigating the role of molecules that control gene expression, such as microRNAs (miR), is an interesting strategy to promote regeneration. The miR-26a promotes neurite outgrowth and axonal regeneration in the peripheral nervous system, by targeting mRNAs that encode proteins related to regeneration pathways. However, the role of miR-26a in axon regeneration in the CNS is still unknown. We aim to test if the overexpression of miR-26a promotes axonal regeneration of CNS neurons.
Methods: We produced recombinant adeno-associated viral (rAAV) vectors expressing miR-26a (rAAV.miR-26a) or EGFP (rAAV.EGFP), as control, to transduce cortical neuron in vitro. Transduction efficiency and neurite regeneration after scratch lesion were evaluated. Then, we performed a bioinformatics evaluation for the mRNA targets of miR-26a.

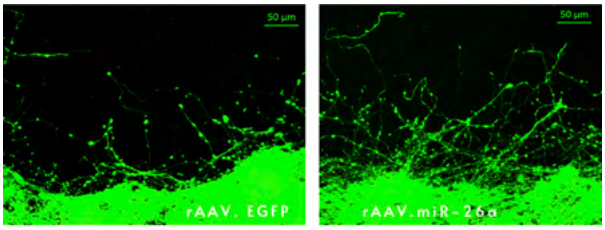


Recombinant adeno-associated viral (rAAV) vectors maps: EGFP (the control) on the left, and miR-26a on the right. Both vectors contains the sequence to express the fluorescent protein EGFP.

Results: Neurons were efficiently transduced with both vectors. Transduction with rAAV.miR-26a increases neurite length and the number of neurites crossing the distance of 200m from the scratch border. The bioinformatics evaluation showed 33 predicted mRNA targets and 30 validated targets of miRNA-26a. These results indicated that miR-26a improves neurite regeneration in vitro, however, further analysis are required to confirm this pro-regenerative effect in vivo.



Transduction efficiency of viral vectors in vitro comparing different types of microscopic images: on the left for both vectors a bright-field light microscopic image and on the right a fluorescence light microscopic image. The vectors worked properly.



Scratch lesion essay: the group transduced with rAAV.miR-26a compared to rAAV.EGFP had an increase in neurite length and in the number of neurites crossing the distance of 200m from the scratch border.

Conclusion: This study could identify novel therapeutic targets to promote regeneration in the CNS.
Disclosure: The authors declare that they have no conflicts of interest.

OPR-117

Corticosterone in acute traumatic brain injury in rats: association with immediate seizures and neuroinflammation

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Background and aims: Corticosterone modulates hippocampal activity, neurogenesis, and plays critical role in susceptibility to seizures. We assessed corticosterone level in blood and hippocampus during acute period of traumatic brain injury (TBI) in rats, its relationships with immediate seizures and proinflammatory response in the blood and hippocampus.

Methods: The study was performed on 140 male Wistar rats. TBI was modelled using lateral fluid percussion brain injury. The duration of immediate posttraumatic seizures were analyzed. Interleukin (IL) -1beta, IL-6 and corticosterone in the blood and hippocampus of both hemispheres were measured on days 1, 3, 7, and 14 after TBI using ELISA.

Results: We revealed that time of day significantly affected the semiology of immediate seizures; tonic seizures were more frequent in the afternoon (close to the period of elevated corticosterone in rats). Corticosterone was elevated on days 1, 3, and 14 after TBI in blood and on day 3 in the hippocampus (bilaterally) as compared to sham-operated rats. IL-1beta raised in the ipsilateral hippocampus on day one and in the hippocampus bilaterally on day seven after TBI. Corticosterone in the blood and hippocampus correlated with immediate seizures duration and IL-1beta level in the contralateral hippocampus seven days after TBI.

Conclusion: Corticosterone-dependent mechanisms may be involved in neuroinflammation and late consequences of TBI, including epilepsy, depression and cognitive disturbances. However, immediate seizures may also be associated with glucucorticoid system and posttraumatic brain pathology.

Disclosure: Supported by RFBR, grant 19-015-00258

OPR-118

Effects of single-walled carbon nanotubes on the survival and release of cytokines from stretch-injured astrocytes

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Background and aims: Astrocytes are considered to have an important role in neuronal regeneration following brain injury. Here, we explored the potential of a nanomaterial on the survival and secretory function of astrocytes after trauma. We tested the effects of single-walled carbon nanotubes (SWCNTs), chemically functionalized with poly-m-aminobenzene sulfonic acids (PABS), in an in vitro model of severe traumatic brain injury (TBI).

Methods: Primary mouse astrocytes were severely injured by rapid stretching. Following injury, PABS-SWCNTs were added to the cell culture medium. Injured and non-injured untreated cells were used as the control TBI and sham-treated groups, respectively. Astrocytes' survival rate within the first 24 h and the effects of PABS-SWCNTSs were determined by lactate dehydrogenase (LDH) assay. Cytokine secretion profiles were evaluated at 24 h after stretch by a multiplex array.

Results: Severe injury triggered an increased release of LDH from the astrocytes. Application of PABS-SWCNTs did not alter the LDH levels compared to the results from the injured, untreated cells. Cell injury caused a decrease in the Eotaxin1 and an increase in the SDF-1 alpha levels in the culture medium compared to the non-injured cells. Application of PABS-SWCNTs induced increased secretion of RANTES from the injured astrocytes, related to non-injured and injured untreated cells.

Conclusion: Reported results indicate that PABS-SWCNTs do not affect the survival of astrocytes subjected to severe TBI within the first 24 h. An increase in the release of RANTES from the injured cells, caused by PABS-SWCNTs addition, points to possible effects of this nanomaterial on the function of injured astrocytes.

Disclosure: This research was fully supported by the Croatian Science Foundation grant UIP-2017-05-9517 to KP.

OPR-119

Lateral fluid percussion injury in the rat instigates early T-cell infiltration in the ipsilateral parietal cortex

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Background and aims: Traumatic brain injury (TBI) represents a burden to healthcare due to limited management options and as well as long-term consequences, which are underrepresented and contribute to naming TBI a "silent epidemic". Neuroinflammation appears to have a significant role in the development of secondary brain injury, involving processes affecting both resolution and persistence of inflammation. The purpose of this study was to elucidate the early activation of the immune cell-mediated response in an experimental model of TBI.
Methods: Lateral fluid percussion injury (LFPI), a TBI model causing both focal cortical lesion and diffuse cerebral damage, was induced in adult male Wistar rats that were sacrificed at 1, 3, or seven days following the procedure. For the control group, we used the animals sacrificed at one day after sham injury. Markers of the cellular arm of adaptive immunity were evaluated by quantitative and qualitative immunohistochemical analyses of the brain tissue.
Results: The results of this study demonstrated the invasion of CD3+, CD4+, and CD8+ cells in the ipsilateral cortices of injured animals. The number of CD3+ cells in this brain region was highest on day one after the trauma and decreased thereafter. CD4+ cells were most abundantly present in the cortex three days after the injury. Invasion of CD8+ cells was also noted in the cortex but also in the subpial space ipsilaterally.
Conclusion: Reported results show that LFPI elicits a cellular immune response within the first week following TBI, which could exacerbate secondary posttraumatic effects and determine recovery outcomes.
Disclosure: This work was supported by the University of Rijeka under the projects uniri-biomed-18-204 and 13.06.1.1.09 to GŽ.

OPR-120

Modulating Balance with Galvanic Vestibular Stimulation in Traumatic Brain Injury Patients

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Background and aims: Impaired balance, mainly a vestibular ataxia, affects 80% of patients with moderate-to-severe acute traumatic brain injury (TBI). Although vestibular ataxia improves over time post-TBI, no interventions have yet been shown to accelerate patient's balance recovery. Neuromodulation by galvanic vestibular stimulation (GVS) may itself or in conjunction with physical therapy, accelerate the balance recovery of TBI patients. We performed a mechanistic, randomised and double-blinded, sham-controlled study exploring the effect of GVS on imbalance in TBI patients.
Methods: We administered bipolar noisy GVS (frequency 0-30Hz) through anodes and cathodes placed on the mastoids of seven TBI patients and four healthy controls (HC). Subjects stood on a soft-foam surface, placed upon a 'balance' or force platform for 120 seconds, with eyes closed. Either anodal or sham stimulation was applied for the first and last 30 seconds of the balance task, in randomised order.
Results: The sway parameters of six TBI subjects reduced when compared to sham, with amplitudes between 100-300uA (n=4) and 500–600uA (n=2). The average sway RMS, path and 95% confidence ellipse area of the subject's movement reduced compared to sham by (Mean (± SEM; p-value) 28.86% (2.57; $p<0.01$), 4.24% (2.65; $p>0.05$) and 41.21% (5.07; $p<0.05$), respectively.
Conclusion: This is the first demonstration of noisy GVS in patients with TBI. Our work demonstrates GVS may have a role in balance modulation in TBI. Future work will assess possible brain mechanisms involved in noisy GVS upon patients' balance.
Disclosure: Nothing to disclose.

Cerebrovascular diseases

OPR-127

Etiology, functional outcome and recurrent events in non-traumatic intracerebral hemorrhage

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Background and aims: Knowledge about different etiologies of non-traumatic intracerebral hemorrhage (ICH) and their outcomes is scarce.

Methods: We assessed prevalence of pre-specified ICH etiologies and their association with outcomes in consecutive ICH patients enrolled in the prospective Swiss Stroke Registry (2014–2019).

Results: We included 2,650 patients (mean age 72 years (SD 14), 46.5% female, median NIHSS 8; IQR 3–15). Etiology was as follows: hypertension: 1,238 patients (46.7%); unknown: 566 patients (21.4%); antithrombotic therapy: 227 patients (8.6%); cerebral amyloid angiopathy (CAA): 217 patients (8.2%); vascular cause: 128 patients (4.8%); other determined etiology: 274 patients (10.3%). At three months, 880 patients (33.2%) were functionally independent and 664 had died (25.1%). ICH due to hypertension had a higher odds of functional independence (aOR 1.33, 95%CI 1.00–1.77, p=0.05) and lower mortality (aOR 0.64, 95%CI 0.47–0.86, p=0.003). ICH due to antithrombotic therapy had higher mortality (aOR 1.62, 95%CI 1.01–2.61, p=0.045). 4.2% of patients had cerebrovascular events within three months. The rate of ischemic stroke was higher than that of recurrent ICH in all etiologies but CAA and unknown etiology. CAA had high odds of recurrent ICH (aOR 3.38, 95%CI 1.48–7.69, p=0.004) while the odds was lower in ICH due to hypertension (aOR 0.42, 95%CI 0.19–0.93, p=0.031).

Conclusion: Although hypertension is the leading etiology of ICH, other etiologies are frequent. One third of ICH patients are functionally independent at three months. Except for patients with presumed CAA, the risk of stroke within three months of ICH was higher than the risk of recurrent hemorrhage.

Disclosure: M.B. Goeldlin: grants from SAMW/Bangerter-Rhyner-Foundation (YTCR 13/18), Swiss Stroke Society, Mittelbauvereinigung at University of Bern, and a congress support from Pfizer, outside of the submitted work.

OPR-128

Phenotypes of chronic covert brain infarction in first-ever ischemic stroke patients – a cohort study

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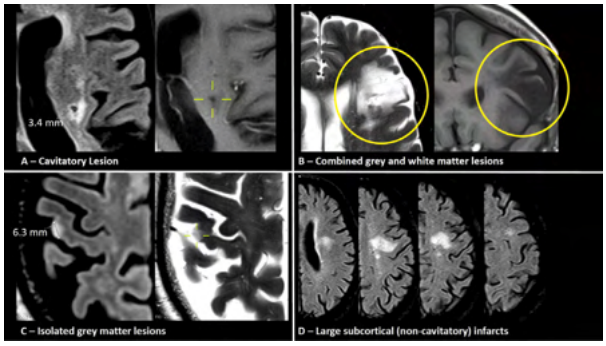
[1] Department of Neurology, Bern, Switzerland, [2] Department of Neuroradiology, Bern, Switzerland, [3] Neuroimaging Sciences, University of Edinburgh, United Kingdom, [4] Department of Cardiology – Rhythmology, Bern, Switzerland

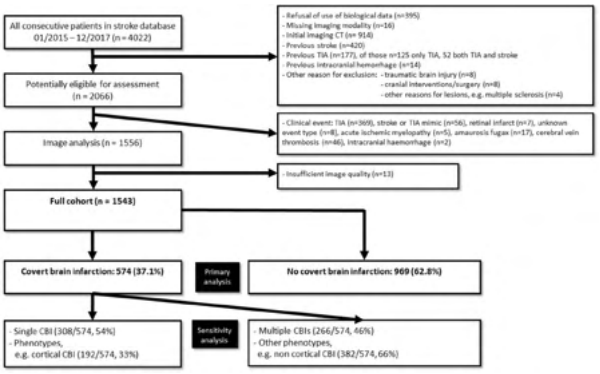
Background and aims: To assess the rate of chronic brain infarctions (CBI) in patients with acute ischemic stroke (AIS) and to describe their phenotypes and diagnostic value.

Methods: This is a single-center cohort study including 1546 consecutive patients with first-ever AIS on MRI imaging from 01/2015–12/2017. The main study outcomes were CBI phenotypes, their relative frequencies, location and association with vascular risk factors.

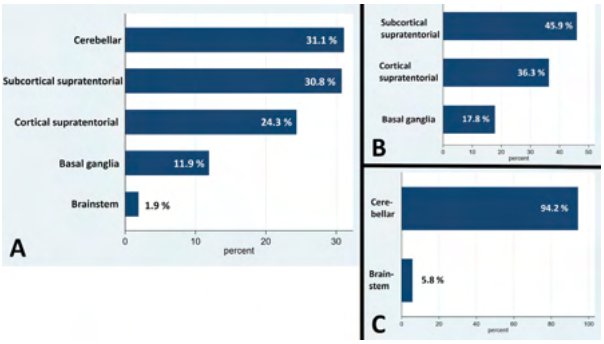


(A) Cavitatory lesions. (B) Combined gray and white matter lesions. (C) Isolated gray matter lesions. (D) Large subcortical (non-cavitatory) infarcts.

Results: Any CBI was present in 574/1546 (37%,95%CI 35–40%) of patients with a total of 950 CBI lesions. The most frequent locations of CBI were cerebellar in 295/950 (31%), subcortical supratentorial in 292/950 (31%), and cortical in 213/950 (24%). CBI phenotypes included cavitatory lesions (49%), combined gray and white matter lesions (30%), gray matter lesions (13%) and large subcortical infarcts (7%). Vascular risk profile and white matter hyperintensities severity (19% if no WMH, 63% in severe WMH, p<0.001) were associated with presence of any CBI. Atrial fibrillation was associated with cortical lesions (aOR 2.032, 95%CI 1.041–3.967)Median NIHSS scores on admission were higher in patients with an embolic CBI phenotype (median NIHSS 5,[2-10],p=0.025).



Study flow chart. TIA = transient ischemic attack, CBI = Covert brain infarction



Conclusion: CBI were present in more than a 3rd of patients with 1st AIS. Their location and phenotypes as determined by MRI were different from previous studies using CT imaging. Among patients suffering AIS, those with additional CBI represent a vascular high-risk subgroup and the association of different phenotypes of CBIs with differing risk factor profiles potentially points towards discriminative AIS etiologies.

Disclosure: No disclosures

OPR-129

Dissociated deficits in the sensorimotor control of torques with the ipsilesional hand of chronic stroke patients

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Background and aims: To safely lift objects without tilting, arising torques due to asymmetric weight distributions must be anticipated and compensated already at lift-off. Previous studies showed that anticipatory force scaling even with the ipsilesional hand may be impaired after stroke. However, anticipatory torque control in object manipulation has not yet been studied in stroke survivors.
Methods: Here, we asked 13 patients with chronic left hemispheric stroke (SL group) and nine patients with right hemispheric stroke (SR group) to use their ipsilesional hand to grasp and lift an object whose center of mass (CoM) could be changed by either varying the position of a hidden weight (no cues condition) or the position of the grip-handle (visual cues condition). CoM changes either occurred after blocks of eight trials or randomly.
Anticipatory torque compensation of stroke survivors was compared with control groups using the same hand (CL/CR-groups).

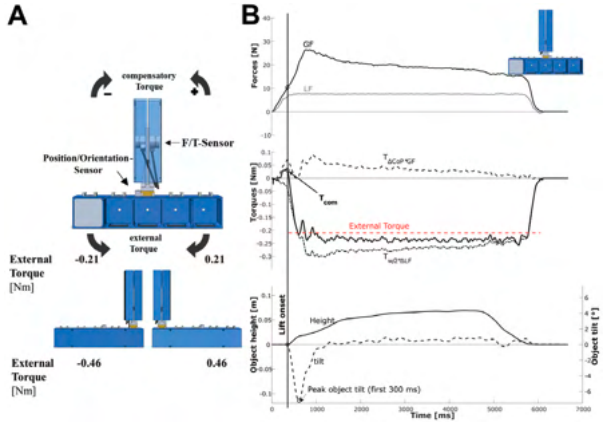

Figure 1: Experimental apparatus and variables. (A) The custom-built grip-device. Upper panel: Variation of the hidden weight position in the 'no cues' condition. Lower panel: variation of the grip handle position (B)

Results: Both stroke groups presented deficits in learning to generate torques by modulating the centers of pressure (CoP) along the grip sides when the hidden weight was placed on the contralesional side but not when placed on the ipsilesional side. In contrast, torque anticipation was similar across groups when visual cues were present and when the CoM was randomly varied.

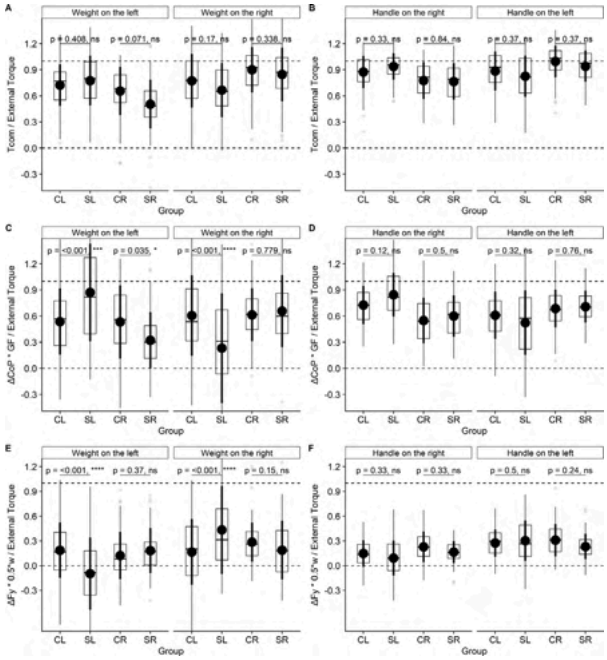

Figure 2: Relative torque ratios for trials 4-8 in the blocked conditions. No cue conditions: panels A, C, D. Visual cues conditions: panels B, D, F.

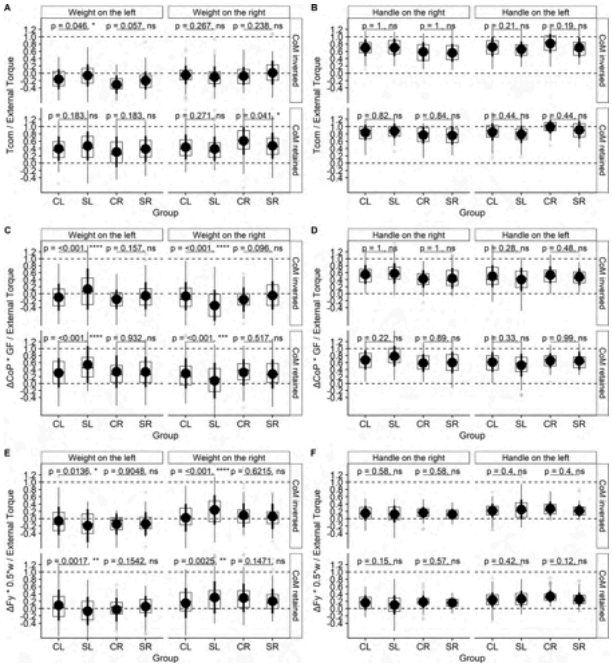

Figure 3: Relative torque ratios for trials 4-8 in the pseudorandom conditions. No cue conditions: panels A, C, D. Visual cues conditions: panels B, D, F.

Conclusion: Our findings provide novel evidence that even in the chronic stage unilateral strokes may impair the sensorimotor control of the anticipatory coordination of finger positions with grip forces selectively for external torques directed towards the contralesional side but spare anticipatory load force partitioning suggesting dissociated neural correlates.
Disclosure: We have no disclosures to declare.

OPR-130

Thrombectomy in Basilar Artery Occlusion

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Background and aims: Recent large multicenter trials investigating thrombectomy (TE) for acute ischemic stroke (AIS) in patients with basilar artery occlusion (BAO) provided conflicting evidence. Our aim was to analyze functional outcome after three months in BAO compared to anterior-circulation large vessel occlusion (ACLVO).
Methods: We analyzed data of all patients enrolled to the Austrian Endostroke Registry. Functional outcome was measured by the modified Rankin Scale. We used propensity score matching to control for imbalances and to compare patients with BAO and ACS. A proportional odds model was applied to estimate the effect of localization (BAO vs ACS). Furthermore, we assessed recanalization rates according to the Thrombolysis in Cerebral Infarction Scale (TICI).
Results: From 2013–2018, 2,288 patients underwent TE for AIS with proximal vessel occlusion, of these 267 with BAO. Follow up data were complete for 2,243 patients; 264 patients with BAO (98.9%). Rates for successful recanalization (TICI2b-3) were high in both BAO (76.9%) and ACLVO (79.5%) and did not differ (p=0.62). We matched 264 patients with BAO and 264 with ACS. In a multivariate proportional odds model we did not detect any difference in functional outcome (OR=1.17, 95%CI 0.85–1.6; p=0.34). In patients with an onset-to-door-time 270 minutes BAO was associated with poor functional outcome (OR=2.55; 95%CI 1.11–5.88; p=0.03).
Conclusion: Functional outcome did not differ after TE in patients with BAO and ACLVO. However, if patients with BAO arrived late, outcome was worse.
Disclosure: Nothing to disclose.

OPR-131

Predicting atrial fibrillation in cryptogenic stroke patients: a score-based approach

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Background and aims: Atrial fibrillation (AF) often remains undiagnosed in patients with cryptogenic stroke (CS), mostly because of limited availability of cardiac long-term rhythm monitoring. Evidence-based pre-selection of CS patients benefiting from such work-up would clearly be of relevance. We therefore sought to develop a clinical risk score to predict AF in this scenario and to evaluate its performance over a 1-year follow-up (FU).
Methods: Our newly proposed risk score comprises variables that have recently been associated with occult AF in CS patients including age, NT-proBNP, electro- and echocardiographic features (supraventricular premature beats, atrial runs, atrial enlargement, left ventricular EF) and brain imaging markers (multi-territory prior cortical infarcts) (range: 0–16 points). To evaluate this, all CS patients admitted to our Stroke Unit from March 2018 to August 2019 had been prospectively followed for AF detection over one year after discharge.
Results: We diagnosed 24 (16%) out of 150 CS patients with AF during FU (detected via ECG-controls, n=18; loop recorder-monitoring, n=6). Our predefined AF Risk Score (cutoff four points, highest Youden's index) had a sensitivity of 92% and a specificity of 68% for the one-year prediction of AF in CS patients. Notably, only two patients with <4 score points were diagnosed with AF later on (negative predictive value: 98%).
Conclusion: We here present a clinical AF risk score for the one-year prediction of AF in CS patients with high sensitivity, reasonable specificity and very high negative predictive value. Generalizability of our score needs to be tested in external cohorts with continuous cardiac rhythm monitoring.
Disclosure: Nothing to disclose.

OPR-132

Off-label alteplase use in anterior spinal artery syndrome – a supportive case report

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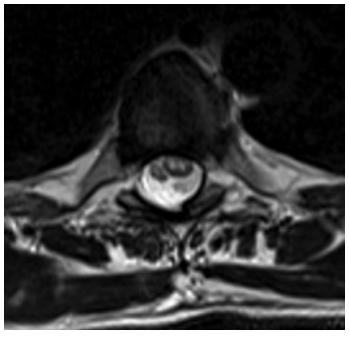
Background and aims: Anterior spinal artery syndrome (ASAS) tends to have a severe functional outcome. Although intravenous thrombolysis with alteplase is well recommended in ischemic stroke, only a few cases of systemic thrombolysis in ASAS have been reported so far, with limited evidence for efficacy or safety.
Methods: Clinical case report of a patient admitted to the emergency room (ER) with ASAS.
Results: We present the case of a 56 year-old male, a former smoker, with a history of diabetes, hypertension and dyslipidemia. He was admitted to the ER for atraumatic chest pain after physical effort, followed by acute lower limb weakness, starting 2.5h before arrival. Neurologic examination showed a flaccid areflexic paraparesis, urinary retention and loss of thermo-algic sensitivity below T10, but preserved vibratory and proprioceptive sensitivity. Thoracolumbar spine CT and CT-angiography revealed no evidence of bleeding, trauma, compressive or intra-axial masses, aortic dissection or arteriovenous malformations. Assuming a probable ASAS of microatheromatous etiology and existing no formal contraindications, the patient, after informed consent, was given 0.9mg/kg alteplase, showing partial clinical improvement about 30 minutes later. A subsequent MRI confirmed the typical T2 "snake-eyes sign", extending from T3 to T11. Intermittent catheterization, antiedematous treatment and secondary prevention with acetylsalicylic acid and atorvastatin were started, with slow progressive improvement. He was transferred to a rehabilitation center, with full motor recovery at discharge three months later.



T2 "snake eyes" sign on thoracic MRI

Conclusion: Despite the absence of formal approval, this case supports that off-label systemic thrombolysis could be safe and useful for the treatment of ASAS – warranting further investigation.
Disclosure: Nothing to disclose.

OPR-133

Abstract withdrawn

OPR-195

Liver fibrosis is associated with atrial fibrillation and worse outcome in large vessel occlusion stroke

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Background and aims: We aimed to explore whether clinically inapparent liver fibrosis is related to neurological outcome, mortality and intracranial haemorrhage in ischemic stroke patients after mechanical thrombectomy.
Methods: We included consecutive patients with anterior circulation large vessel occlusion stroke treated at our centre with mechanical thrombectomy between January 2011 and April 2019 and collected clinical data prospectively. We calculated three established non-invasive liver fibrosis scores: Fibrosis-4 index (FIB-4), Forns index and Easy Liver Fibrosis Test (eLIFT). Main outcomes were postinterventional intracranial haemorrhage, unfavourable functional status (modified Rankin scale scores of 3–6) and mortality three months post-stroke.
Results: In the 465 patients (mean age 69 years, 49.5% female) analysed, FIB-4, Forns index and eLIFT indicated advanced liver fibrosis in 22.6%, 37.6% and 58.7% of patients, respectively. All three indices were associated with unfavourable neurological outcome and mortality three months post-stroke after correction for stroke severity, recanalization status and relevant comorbidities (e.g., Odds Ratio 2.06 for unfavourable outcome in patients with positive FIB-4, 95% CI 1.20–3.55, p=0.009, and Odds Ratio 2.18 for mortality, 95% CI 1.25-3.79, p=0.006). However, liver fibrosis was not related to haemorrhagic transformation or symptomatic intracranial haemorrhage. Atrial fibrillation was more frequent in patients with liver fibrosis (60.6% vs. 36.1% in patients with vs. without positive FIB-4, p<0.001).
Conclusion: Clinically inapparent liver fibrosis (based on simple non-invasive tests) represents an independent risk factor for unfavourable outcome including mortality after stroke thrombectomy. Elevated liver fibrosis indices warrant further hepatological work-up and thorough screening for atrial fibrillation in stroke patients.
Disclosure: Nothing to disclose.

Headache and Pain 2

OPR-134

Long-term Safety and Tolerability of Atogepant: Once Daily Dosing Over one Year for the Preventive Treatment of Migraine

M. Ashina [1], S. Tepper [2], U. Reuter [3], A. Blumenfeld [4], S. Hutchinson [5], J. Xia [6], R. Miceli [6], L. Severt [6], M. Finnegan [6], J. Trugman [6]
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Background and aims: Atogepant is an oral, small molecule, CGRP receptor antagonist in development for the preventive treatment of migraine. We evaluated the safety and tolerability of atogepant over 52 weeks.
Methods: Multicenter, open-label trial (NCT03700320). Adults with migraine were randomized 5:2 to atogepant 60 mg once daily or oral standard-of-care migraine prevention medicine. The primary objective was to assess the safety and tolerability of atogepant. Standard-of-care was included to primarily help contextualize hepatic safety data.
Results: The trial included 744 randomized participants (n=546 atogepant) with 739 in the safety population (n=543 atogepant). Adverse events (AEs) were reported by 67.0% of atogepant-treated participants; 18.0% reported AEs that were considered treatment-related. Most commonly reported AEs (5% of participants) were upper respiratory tract infection (10.3%), constipation (7.2%), nausea (6.3%), and urinary tract infection (5.2%) following atogepant treatment. Serious AEs were reported by 4.4% of atogepant-treated participants; no event was seen in >1 participant and no event was considered treatment-related. Two deaths were reported in atogepant-treated participants (victim of homicide and a group A beta-hemolytic streptococcal sepsis [toxic shock syndrome]); both were considered not related to atogepant. Discontinuation due to AEs was 5.7% following atogepant treatment. Cases of alanine aminotransferase/aspartate aminotransferase levels three times the upper limit of normal were reported for 2.4% of atogepant-treated participants (n=13/531) and 3.2% for standard-of-care (n=6/190). No cases of potential Hy's Law were reported.
Conclusion: Long-term, once daily use of atogepant 60 mg for the preventive treatment of migraine over one year was safe and well-tolerated with no safety concerns identified.
Disclosure: Study was sponsored by AbbVie

OPR-135

Real-world evidence for chronic migraine control in patients receiving treatment with CGRP mAbs and onabotulinumtoxinA

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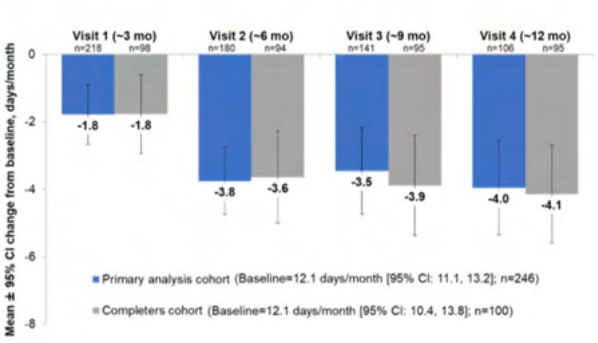
Background and aims: Combining onabotulinumtoxinA and calcitonin generelated peptide monoclonal antibody therapy (CGRP mAbs) could potentially be more effective than either treatment alone for preventing chronic migraine (CM).
Methods: This retrospective, longitudinal chart review included adults with CM treated with ≥2 consecutive onabotulinumtoxinA injections before ≥1 month of onabotulinumtoxinA plus CGRP mAb (erenumab, fremanezumab, or galcanezumab) combination treatment (primary cohort). Safety/tolerability (adverse events [AEs], discontinuations) and outcome measures (monthly headache days [MHDs], migraine-related disability [MIDAS]) were reviewed. Patients who completed ~12 months of onabotulinumtoxinA treatment after initiating CGRP mAb (completers) were evaluated.
Results: Of 300 charts reviewed, 257 were included in the primary cohort (mean age: 50 years; 82% women) and 103 (40%) met criteria for completers. CGRP mAb included erenumab (primary: 78%; completers: 84%), galcanezumab (16%; 11%) and fremanezumab (6%; 5%). In the primary cohort, AEs were reported in 28% of patients; the most common AE was constipation (9%). Mean MHDs were 21.5 and 22.4 days before onabotulinumtoxinA initiation in the primary and completer cohorts, respectively, and 12.1 days before adding CGRP mAb in both cohorts. After ~6 months, positive changes were noted in the primary and completer cohorts: 82% and 83% had decreased MHDs, and 57% and 55% had improved MIDAS (Figure). All reductions were significant given non-overlapping CIs.



CGRP mAb, calcitonin gene–related peptide monoclonal antibody.

Mean change from baseline in monthly headache days during combination therapy with onabotulinumtoxinA and CGRP mAbs

Conclusion: This real-world study of CM patients demonstrated clinically meaningful benefits with onabotulinumtoxinA alone and additive benefits after adding CGRP mAb with no new safety signals. More real-world studies and controlled trials are needed to further quantify potential benefits of this multimodal treatment paradigm.

Disclosure: This study was supported by Allergan (prior to its acquisition by AbbVie).

OPR-136

Consistent efficacy and safety of erenumab in episodic migraine patients during a 5-year, open-label extension study

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[1] Department of Neurology, Danish Headache Center, Rigshospitalet Glostrup, Faculty of Health and Medical Sciences, University of Copenhagen, Denmark, [2] NIHR-Wellcome Trust King's Clinical Research Facility, King's College London, London, United Kingdom, [3] Department of Neurology, Charité Universitätsmedizin Berlin, Berlin, Germany, [4] Jefferson Headache Center, Thomas Jefferson University, Philadelphia, PA, United States, [5] Department of Neurology, Mayo Clinic, Scottsdale, AZ, United States, [6] Amgen Inc., Thousand Oaks, CA, United States

Background and aims: Erenumab demonstrated significant reduction in migraine frequency in short-term studies; however, long-term data are not available. The long-term efficacy and safety of erenumab was evaluated in episodic migraine patients who completed a 5-year open-label treatment phase (OLTP; NCT01952574).

Methods: Following a 12-week placebo-controlled, double-blind treatment period (DBTP), 383 patients continued into the OLTP, receiving erenumab 70mg every four weeks, and increasing to 140mg after a protocol amendment (after ~2 years in OLTP). Overall, 214 patients completed the 5-year OLTP; 138 patients had efficacy data at Week 268 (end of 5-year OLTP) and were included in this analysis.

Results: At Week 268, the mean(SD) change from the DBTP baseline in monthly migraine days (MMD) and monthly acute migraine-specific medication (AMSM) days was 5.3(3.9) and 4.4(3.3), respectively (Table 1). The proportion of patients who achieved ≥50%, ≥75% and 100% reduction in MMD at Week 64/268 was 62%/71%, 41%/47% and 26%/36%, respectively. Clinically meaningful improvements were observed in headache impact test-6TM: 68%/73% of patients achieved ≥5-point reduction from baseline at Weeks 64/268. Exposure-adjusted patient incidence of adverse events (AEs) and serious AEs during OLTP was 91.6 and 2.8 per 100 subject-years, respectively; this was lower than that observed for erenumab 70mg during DBTP. One fatality occurred during the safety follow-up period¬ when no erenumab was administered and was considered unrelated to study drug by the investigator.

Outcomes	Baseline	Week 64	Week 268
Change from the DBTP baseline in MMD	8.5(2.5)	−4.8(3.9)*	−5.3(3.9)**
Change from the DBTP baseline in AMSM	6.2(2.7)	−3.2(3.4)	−4.4(3.3)

Data presented are mean(SD). *Mean of last 4 weeks of 1-year OLTP; ** Mean of last 4 weeks of 5-year OLTP. All patients received erenumab 70mg at Week 64 and 140mg at Week 268.
AMSM, acute migraine-specific medication; DBTP, double-blind treatment phase; MMD, monthly migraine days; OLTP, open-label treatment phase

Study outcomes at the end of 5-year OLTP among completers

Conclusion: Patients receiving erenumab over 5-years demonstrated consistent and sustained response. Safety was comparable to that observed in patients who received erenumab 70mg during the randomised phase of the trial.
Disclosure: Amgen Inc., Thousand Oaks, CA, funded this study. Erenumab is co-developed by Amgen and Novartis. A detailed disclosure from each author will be included in the oral/poster presentation.

OPR-137

Brain structural MRI predicts outcome of surgical treatment in trigeminal neuralgia

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Background and aims: To determine structural magnetic resonance imaging (MRI) alterations occurring in trigeminal neuralgia (TN) patients and to assess the predictive capability of abnormal neuroimaging findings for pain-maintenance and surgical outcomes.
Methods: 30 patients with idiopathic or classic TN, who underwent Gamma Knife radiosurgery and were followed for at least 24 months, were retrospectively analysed. Patients' structural pre-treatment MRI, and their pre- and post-operative clinical features were investigated. 15 age- and sex-matched healthy controls without any pain condition were also enrolled. Cortical thickness and subcortical gray matter (GM) atrophy were assessed in TN patients relative to controls, and among patient subgroups according to treatment outcomes (initial responders/non-responders, recurrence/long-lasting pain relief). MRI predictors of treatment outcomes were also explored.
Results: Cortical thinning of temporal, prefrontal, cingulate and somatosensory areas bilaterally were found in TN patients relative to controls. No significant cortical thickness and GM volume differences were found when TN initial (6 months after treatment) responder and non-responder patients were compared. Patients who experienced TN recurrence after initial pain relief were characterized by thicker parahippocampal and temporal lobe cortex bilaterally and higher volume of right amygdala and hippocampus compared to patients with
long-lasting pain relief at last follow-up. Furthermore, baseline cortical thinning of right parahippocampal, left fusiform, left middle temporal cortex values and disease duration were associated with poor outcome after treatment at last follow-up in all TN patients ($R2= 0.57$, $p < 0.001$).
Conclusion: The study provides novel insights into TN brain structural alterations, which might contribute to TN development and its maintenance.
Disclosure: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

OPR-138

NMA of migraine day reductions with CGRP pathway-targeting mAbs in migraine patients with multiple preventive failures

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Background and aims: Head-to-head randomized, controlled trials(RCT) comparing the efficacy of monoclonal antibodies(mAbs) targeting the calcitonin gene-related peptide(CGRP) pathway for migraine preventive treatment are not available. This network meta-analysis(NMA) assessed the relative efficacy of mAbs targeting the CGRP pathway for reducing average number of monthly migraine days(MMD) in patients with chronic or episodic migraine(CM or EM) with multiple prior treatment failures.

Methods: A systematic literature review(SLR) was conducted to identify placebo-controlled RCT evaluating the effects of fremanezumab quarterly(675mg), fremanezumab monthly(225mg), galcanezumab(120mg), erenumab(140mg), and erenumab(70mg) on MMD in CM or EM patients with 2–4 and ≥3 prior preventive treatment failures. A Bayesian NMA was conducted to assess change from baseline in MMD over weeks 1–12 in patients with 2–4 and ≥3 prior treatment failures.

Results: The SLR identified six RCT for EM and four for CM for patients with ≥2 prior failures. Compared with placebo, median reductions in MMD among EM patients with 2–4 prior treatment failures were significantly greater for fremanezumab quarterly (3.10[95% credible interval(CrI):1.89,4.31]), fremanezumab monthly (3.20 [1.99,4.41]), galcanezumab 120mg (2.61[1.85,3.39]), and erenumab (70mg:0.87[1.34,3.06]; 140mg:1.87[1.27,2.47]). Reductions were numerically but not statistically significantly greater for fremanezumab versus erenumab(Table). There were no significant differences for fremanezumab versus erenumab or galcanezumab in the CM and CM/EM groups with 2–4 prior failures or the EM, CM, and CM/EM groups with ≥3 prior failures (Table).

Table. Comparison of Changes in MMD From Baseline Over Week 1-12 Among Patients With 2-4 and ≥3 Prior Migraine Preventive Treatment Failures

Comparison for MMD, median (95% CrI)	Fremanezumab quarterly	Fremanezumab monthly	Galcanezumab 120 mg	Erenumab 140 mg	Erenumab 70 mg
2-4 prior failures					
EM					
Vs placebo	3.10 (1.89, 4.31)	3.20 (1.99, 4.41)	2.61 (1.85, 3.39)	1.87 (1.27, 2.47)	0.87 (−1.34, 3.06)
Vs erenumab 70 mg	2.22 (−0.28, 4.73)	2.33 (−0.16, 4.84)	1.74 (−0.58, 4.08)	1.00 (−1.17, 3.19)	—
Vs erenumab 140 mg	1.22 (−0.12, 2.57)	1.32 (−0.02, 2.69)	0.73 (−0.24, 1.72)	—	—
Vs galcanezumab 120 mg	0.49 (−0.96, 1.92)	0.60 (−0.85, 2.01)	—	—	—
CM					
Vs placebo	3.09 (1.84,4.37)	3.70 (2.45, 4.96)	4.07 (2.85, 5.31)	3.90 (3.01, 4.79)	2.50 (1.61, 3.39)
Vs erenumab 70 mg	0.59 (−0.94, 2.14)	1.20 (−0.35, 2.76)	1.57 (0.08, 3.09)	1.40 (0.44, 2.35)	—
Vs erenumab 140 mg	−0.80 (−2.34, 0.73)	−0.20 (−1.74, 1.35)	0.17 (−1.32, 1.68)	—	—
Vs galcanezumab 120 mg	−0.97 (−2.73, 0.78)	−0.37 (−2.12, 1.39)	—	—	—
CM/EM					
Vs placebo	3.10 (2.27, 3.93)	3.50 (2.67, 4.33)	3.10 (2.25, 3.94)	N/A	N/A
Vs galcanezumab 120 mg	−0.00 (−1.18, 1.18)	0.40 (−0.77, 1.59)	—	N/A	N/A
≥3 prior failures					
EM					
Vs placebo	3.98 (1.84, 6.13)	3.98 (1.86, 6.07)	2.90 (1.09, 4.70)	N/A	N/A
Vs galcanezumab 120 mg	1.09 (−1.71, 3.90)	1.09 (−1.70, 3.82)	—	N/A	N/A
CM					
Vs placebo	2.90 (1.33, 4.46)	3.00 (1.41, 4.58)	5.18 (3.27, 7.12)	N/A	N/A
Vs galcanezumab 120 mg	−2.29 (−4.79, 0.22)	−2.18 (−4.71, 0.33)	—	N/A	N/A
CM/EM					
Vs placebo	3.39 (2.05, 4.74)	3.49 (2.15, 4.81)	4.49 (2.57, 6.45)	N/A	N/A
Vs galcanezumab 120 mg	−1.11 (−3.47, 1.24)	−1.00 (−3.36, 1.31)	—	N/A	N/A

MMD, monthly migraine days; EM, episodic migraine; CrI, credible interval; CM, chronic migraine; N/A, not available.

Table. Comparison of Changes in MMD From Baseline Over Week 1–12 Among Patients With 2–4 and 3 Prior Migraine Preventive Treatment Failures

Conclusion: Fremanezumab, galcanezumab, and erenumab showed statistically significant reductions in MMD versus placebo in migraine patients with multiple prior preventive failures. No statistically significant differences were noted for fremanezumab versus erenumab or galcanezumab.

Disclosure: This network meta-analysis (NMA) was funded by Teva Pharmaceuticals.

OPR-139

Pooled analysis of efficacy of fremanezumab for reducing disability and acute medication overuse in migraine patients

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Background and aims: Migraine patients who overuse acute headache medications may experience higher levels of pain and disability. Fremanezumab, a fully-humanized monoclonal antibody (IgG2a) that selectively targets calcitonin gene-related peptide (CGRP), has proven efficacy for migraine prevention in adults. These pooled analyses evaluated fremanezumab in a subgroup of patients who overused migraine-specific acute medication (triptan or ergot use 10 days/month) at baseline (MO subgroup).

Methods: These pooled analyses included data from three clinical trials (HALO episodic migraine [EM], HALO chronic migraine [CM], and FOCUS), in which patients were randomized to 12 weeks of double-blind treatment with quarterly fremanezumab, monthly fremanezumab, or placebo. Assessments included changes from baseline in monthly migraine days (MMDs), days of acute headache medication use, and disability outcomes (6-item Headache Impact Test [HIT-6] and Migraine Disability Assessment [MIDAS]), as well as the proportion of patients who reverted to not overusing acute medication in the MO subgroup.

Results: Of the pooled population of 2,842 patients, 749 were included in the MO subgroup. Quarterly and monthly fremanezumab treatment provided significant reductions in MMDs and monthly days of acute medication use versus placebo (Table). Fremanezumab treatment also resulted in significant reductions in HIT-6 and MIDAS scores versus placebo (Table). A significantly higher proportion of patients reverted to no medication overuse with fremanezumab treatment versus placebo (Table).

Table. Efficacy, Disability, and Medication Use in Patients Overusing Acute Migraine-specific Medications at Baseline

Outcome	Placebo (n = 240)	Quarterly fremanezumab (n = 270)	Monthly fremanezumab (n = 239)
Change from baseline in MMDs during 12 weeks, LSM (SE)	−1.7 (0.37)	−4.8 (0.37)[a]	−5.4 (0.38)[a]
Change from baseline in monthly days with acute medication use during 12 weeks, LSM (SE)	−1.6 (0.36)	−4.9 (0.35)[a]	−5.4 (0.37)[a]
Change from baseline in HIT-6 score during 12 weeks, LSM (SE)[b]	−2.7 (0.55)	−5.1 (0.51)[c]	−6.7 (0.52)[a]
Change from baseline in MIDAS score during 12 weeks, LSM (SE)[d]	−9.1 (4.43)	−23.3 (4.42)[a]	−31.2 (4.65)[a]
Patients reverting to no medication overuse at 12 weeks, n (%)	67 (28)	143 (53)[a]	145 (61)[a]

MMDs, monthly migraine days; HIT-6, 6-item Headache Impact Test; MIDAS, Migraine Disability Assessment.
[a]$P < 0.0001$ versus placebo.
[b]Pooled HALO CM/FOCUS population: placebo, n = 211; quarterly fremanezumab, n = 246; monthly fremanezumab, n = 223.
[c]$P = 0.0002$ versus placebo.
[d]Pooled HALO EM/FOCUS population: placebo, n = 141; quarterly fremanezumab, n = 151; monthly fremanezumab, n = 137.
[e]$P = 0.0040$ versus placebo.

Table. Efficacy, Disability, and Medication Use in Patients Overusing Acute Migraine-specific Medications at Baseline

Conclusion: Treatment with fremanezumab was effective and resulted in significant reductions in disability and overuse of acute migraine-specific abortive medications, demonstrating the benefits of fremanezumab in those with overuse of acute migraine-specific medications.

Disclosure: Studies and analyses were funded by Teva Pharmaceuticals.

COVID-19 2

OPR-140

CNS and PNS complications of COVID-19: a prospective tertiary center cohort with 3-month follow-up

V. Nersesjan [1], M. Amiri [2], A. Lebech [3], C. Roed [3], H. Mens [3], L. Russell [4], L. Fonsmark [4], M. Berntsen [5], S. Sigurdsson [5], J. Carlsen [6], A. Langkilde [6], P. Martens [6], E. Lund [7], K. Hansen [2], B. Jespersen [8], M. Folke [9], P. Meden [9], A. Hejl [9], C. Warmberg [10], M. Benros [11], D. Kondziella [2]

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Background and aims: To systematically describe CNS and PNS complications in hospitalized COVID-19 patients.
Methods: We conducted a prospective, observational study of adult patients from a tertiary referral center with confirmed COVID-19. All patients were screened daily for neurological and neuropsychiatric symptoms during admission and discharge. Three-month follow-up data were collected using electronic health records. We classified complications as caused by SARS-CoV-2 neurotropism, immune-mediated or critical illness-related.
Results: From April-September 2020, we enrolled 61 consecutively admitted COVID-19 patients, 35 (57%) of whom required ICU management for respiratory failure. Forty-one CNS/PNS complications were identified in 28 of 61 patients and were more frequent in ICU compared to non-ICU patients. The most common CNS complication was encephalopathy (n=19, 31.1%), which was severe in 13 patients (GCS 12), including eight with akinetic mutism. Length of ICU admission was independently associated with encephalopathy (OR=1.22). Other CNS complications included ischemic stroke, a biopsy-proven acute necrotizing encephalitis, and transverse myelitis. The most common PNS complication was critical illness polyneuromyopathy (13.1%), with prolonged ICU stay as independent predictor (OR=1.14). Treatment-related PNS complications included meralgia paresthetica. Of 41 complications in total, three were para/post-infectious, 34 were secondary to critical illness or other causes, and four remained unresolved. Cerebrospinal fluid was negative for SARS-CoV-2 RNA in all five patients investigated.

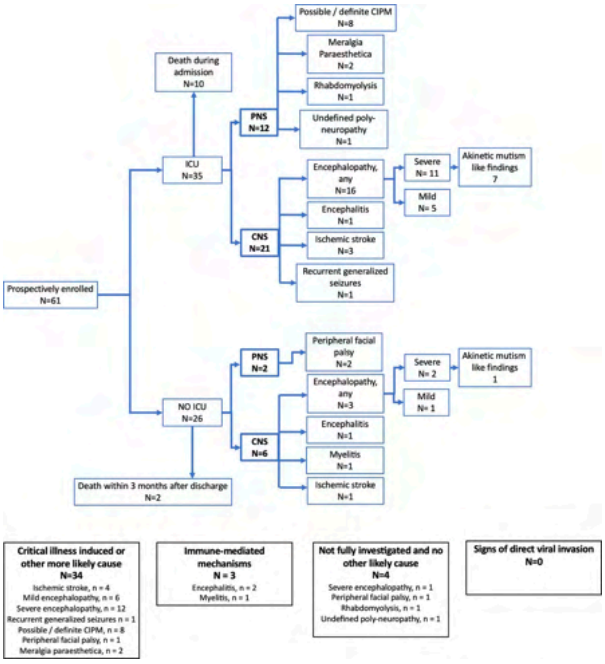

FIGURE 1 – Flow-chart of patient inclusion and observed neurological complications

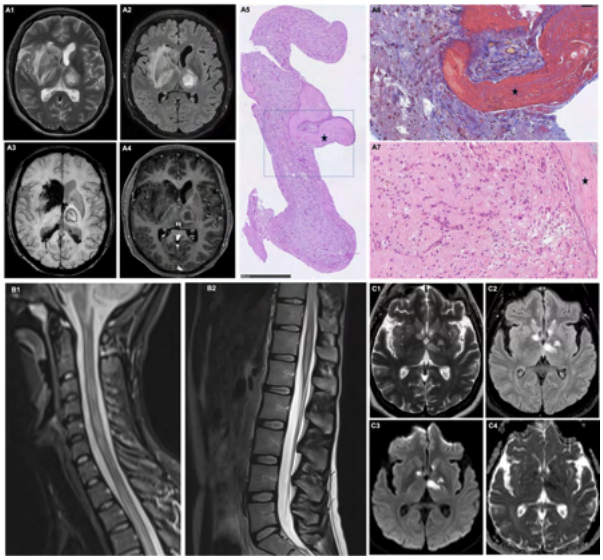

FIGURE 2 – Brain and spinal imaging and histopathology from probable COVID-19 encephalitis and myelitis

Conclusion: CNS/PNS complications were common in hospitalized COVID-19 patients, particularly in the ICU, and often attributable to critical illness. When COVID-19 was the primary cause for neurological disease, no signs of viral neurotropism were detected, but laboratory changes suggested autoimmune-mediated mechanisms.
Disclosure: The authors declare that they have no conlicts of interest.

OPR-141

Neuro-COVID in the northern Portuguese population

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Background and aims: COVID-19 related acute neurological phenotypes have been reported in over 30% of hospitalized patients. However, multicentric studies providing a population-based overview are still lacking.
Methods: We conducted a retrospective multicentric study in five hospitals in Northern Portugal, between March 1st and June 30th 2020. Patient e-records were systematically revised using a standardized form to identify neurological manifestations stratified by type and severity.
Results: From a total of 13,144 persons diagnosed with COVID-19 in the northern region, 2,795 (21.3%) required hospitalization. We reviewed a sample of 1,261 (45.1%) hospitalized patients and found a rate of 362 neurological manifestations per 1000 admitted COVID-19 patients, estimating a total of 1009 hospitalized patients with a neurological manifestation in the Northern Region. Patients with neurologic manifestations were younger (p=0.002), and the most frequent neurological symptoms were headache (13.4%), delirium (10.1%) and impairment of consciousness (9.7%). We observed a rate of 7.8 severe neurological events per every 1000 COVID-19 infected patients, including stroke, seizures, Guillain-Barre syndrome and myelopathy. The fatality among patients with neurological manifestations was 19.8%, and 15.6% had a modified Rankin Scale of 4-5 at hospital discharge.
Conclusion: We characterized the population of hospitalized COVID-19 patients from the northern region of Portugal and found that neurological symptoms are common and associated with a high degree of disability. CNS involvement with criteria for in-hospital admission was observed in a significant proportion of patients. Neurology support is highly relevant in the multidisciplinary care of COVID-19 patients.
Disclosure: This work was partially funded by "Fundação para a Ciência e Tecnologia", Grant nº229 (RESEARCH4 COVID-19). No conflicts of interest to report.

OPR-142

Brain metabolism and persistent olfactory deficits after SARS-CoV-2 infection: an FDG-PET study

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Background and aims: Coronavirus disease 2019 (COVID-19) due to SARS-CoV-2 infection has been associated with a number of neurological complications, including persistent hyposmia. Despite its relative frequency the neural bases of hyposmia post-SARS-Cov2 infection are to date poorly understood.
Methods: 22 patients (12 males and 10 females; mean age 64±10.5 years, range 35–79) underwent whole-body [18] F-FDG-PET including a dedicated brain acquisition following their recovery after SARS-CoV-2 infection. Patients that previously required mechanic ventilation or showed severe respiratory distress syndrome due to SARS-CoV-2 infection were excluded given the potential independent effect of these clinical scenarios on brain metabolism. Among the enrolled patients, presence of isolated persistent hyposmia, as assessed with the smell diskettes olfaction test, was shown in fourteen subjects. A voxelwise analysis was used to identify brain regions of relative hypomebolism in hyposmic patients compared to a group of 61 age- and sex-matched healthy controlsStructural connectivity of these regions was assessed with the BCB toolkit.
Results: Relative hypometabolism was demonstrated in bilateral parahippocampal and fusiform gyri and in left insula in hyposmic patients with respect to controls. Structural connectivity maps showed the involvement of the bilateral longitudinal fasciculi.
Conclusion: Here we provide the first evidence of cortical hypometabolism in patients with isolated persistent hyposmia after SARS-CoV-2 infection without an history of severe respiratory distress. [18]F-FDG-PET may play a role in the identification of long-term brain functional sequelae of COVID-19.
Disclosure: Silvia Morbelli and Flavio Nobili have received speaker honoraria from G.E. Healthcare. Matteo Pardini receives research support from Novartis. All other authors declare no conflict of interest.

OPR-143

Primary intracerebral haemorrhage during SARS-CoV-2 outbreak

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Background and aims: Mounting data has been published as to the impact of SARS-CoV-2 on cerebrovascular events, particularly on ischemic strokes. Our study addresses the clinical course of patients with cerebral haemorrhage and simultaneous SARS-CoV-2 infection, paying particular attention to both SARS-CoV-2 positive and negative patients hospitalized during the pandemic.

Methods: The Italian Society of Hospital Neurosciences (SNO) promoted a multicentre, retrospective, observational study (SNO-COVID-19), involving 20 Neurology Units in Northern Italy. Data were collected on patients consecutively admitted to neurological departments, from March 1st to April 30th with cerebrovascular diseases, occurring either at home or during hospitalization for other causes.

Results: 949 patients were enrolled (average age 73.4 years; 52.7% males); 135 patients had haemorrhagic stroke and 127 (13.4%) had a primary ICH. Only 16 patients with ICH (12.6%) had laboratory confirmed SARS-CoV-2 infection, clinically expressed or not. SARS-CoV-2 related pneumonia or respiratory distress, lobar location and previous antiplatelet or anticoagulant treatment were the only factors significantly associated with increased mortality in ICH. SARS-CoV-2 infection, regardless of respiratory involvement, led to a non-significantly increased risk of in-hospital death.

Conclusion: Our study confirms that age, ICH location and previous antiplatelet or anticoagulant treatment are predictors of in-hospital death. Unlike ischemic stroke, ICH in SARS-CoV-2 patients led only to a slight increase in mortality, mainly due to respiratory involvement.

Disclosure: The authors declare that they have no conflict of interest

OPR-144

COVID-19 in patients with dementia : clinical features and predictive factors of mortality in a cohort of 125 patients

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Background and aims: There is limited evidence on the characteristics and outcome of COVID-19 in patients with dementia. We report a cohort study on 125 patients with dementia hospitalized for a confirmed SARS-CoV-2 infection.

Methods: We conducted a prospective study in two gerontologic Covid Units in Paris, France, from March 14th 2020 to May 7th 2020. Patients with dementia hospitalized for confirmed infection were systematically enrolled. A binary logistic regression analysis was performed to identify factors associated with mortality at 21 days.

Results: We included 125 patients. Median age was 86 (IQI 82–90); 59.4% were female. Most common causes of dementia were Alzheimer's disease, mixed dementia and vascular dementia. 67.2% had two comorbidities; 40.2% lived in a long-term care facility. The most common symptoms at COVID-19 onset were confusion and delirium (79%), asthenia (74.4%) and fever (70.5%) before polypnea (49.6%) and desaturation (48.8%). Falls were frequent at the initial phase of the disease (34%). The fatality rate at 21 days was 22.4%. Chronic kidney disease and CRP at admission were independent factors of death. Persisting confusion, mood and behavioral disorders were observed in survivors (19.2%).

Conclusion: In demented patients, SARS-CoV-2 was frequently revealed by confusion and asthenia and was associated with severe outcome. COVID19 testing should be considered in front of any significant change from baseline in patients with dementia.

Disclosure: No conflict of interest

Movement disorders: Clinical

OPR-075

Ferroptosis, a recently identified cell death, as a therapeutic target for Parkinson's disease

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Background and aims: Ferroptosis is a new form of regulated cell death characterized by the iron-dependent accumulation of lipid hydroperoxides to lethal levels, which is a key marker of this pathway. Recently, we demonstrated that ferroptosis is prevalent in pro-oxidant models of Parkinson's disease. Furthermore, several reports have characterized LOXs as key drivers of lipid peroxidation during ferroptosis. We aim to determine in a cell model, neuroprotective effects of targeting lipoxygenases (LOXs), central players in Ferroptosis.
Methods: By qPCR, we examined the expression pattern of LOXs in LUHMES cells, a human neuronal precursor derived cell line, which can be differentiated into mature dopaminergic neurons. To determine whether the inhibition of LOXs confer resistance to ferroptosis, we treated LUHMES cells with lipoxygenases inhibitors or silenced LOXs genes using siRNA. Then we induced ferroptosis with two inducers, RSL3 and Erastin. Cell death was measured after 24 hours of treatment by rezasurin assay and levels of lipid peroxidation were detected by flow cytometry using a lipophilic reactive oxygen species sensor (Bodipy 581/591 C11)
Results: We have observed that selective LOXs inhibitors conferred a high neuroprotection against RSL3 and Erastin-induced ferroptotic cell death. Similar results were obtained by decreasing the expression levels of genes detected par qPCR (15-LOX, 15B-LOX and 12B-LOX). Levels of lipid peroxidation in response of RSL3 or Erastin were equally reduced by pharmacologic or genetic inhibition of LOXs.
Conclusion: The implication of ferroptosis in neurodegeneration of PD offers wide possibilities of neuroprotective strategies and targeting lipoxygenases in particular seems to be a promising one.
Disclosure: The authors have nothing to declare.

OPR-092

Parkinson's disease Mobile Application v2 detects potential disease modifying effect of prasinezumab

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Background and aims: Digital health technologies (DHTTs) enable remote and frequent monitoring of motor symptoms in Parkinson's disease (PD), and may more readily detect effects of disease modifying therapies compared to infrequently administered clinical scales. We report the effects of prasinezumab, an anti-alpha synuclein monoclonal antibody, on motor disease progression measured with the Roche PD Mobile Application v2 (ph2 PASADENA study; NCT03100149).
Methods: 316 individuals recently diagnosed with PD were randomized to placebo, 1500mg and 4500mg dose groups. All received a smartphone/watch, performed daily active motor tests, and carried/wore devices throughout the day. Seventeen pre-specified sensor features were aggregated over fortnights. Linear mixed effect models with random slopes fit each feature's change from baseline. Random mixed effects models modeled nonlinear data. Effects of interest were defined as $p<0.2$, and multiple comparison correction was applied at 15% false discovery rate.
Results: Features from speeded tapping, hand-turning, U-turning and spontaneous hand gestures showed treatment effects favoring prasinezumab. One feature (spiral drawing accuracy/time) showed an effect favoring placebo, with divergent results for drawing accuracy and time. Tremor, Speech, Sustained Phonation and SDMT features did not differ across groups. Two features survived FDR-correction, both favoring prasinezumab: least affected side speeded tapping, and gesture power in daily life reflecting an impact on patients' spontaneous motor behavior in daily life. Additional subgroup analyses will be presented.
Conclusion: In individuals with PD treated with prasinezumab, daily quantification of motor severity via a DHTT showed a divergence of slopes, which is consistent with an effect of disease progression.
Disclosure: This research has been funded by F. Hoffmann-La Roche AG and Prothena Biosciences Inc.

OPR-093

Assessment of brain concentration of UCB0599, in development for Parkinson's disease (PD), in humans using PET

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Background and aims: Alpha-synuclein misfolding is one of the best genetically and pre-clinically validated early steps in the cascade leading to loss of dopaminergic neurons, the hallmark of PD. UCB0599, an orally administered, brain penetrant, small molecule inhibitor of alpha-synuclein monomer misfolding, is under investigation for the potential to slow the progression of PD. The safety, tolerability, pharmacokinetics and brain biodistribution of UCB0599 were assessed using PET in a phase 1 study.

Methods: Healthy volunteers (aged 25–55 years; n=4) underwent PET/CT twice on Day 1: once after an intravenous micro-dose (maximum of 10ug) of 11C-UCB0599, and once after an intravenous micro-dose of 11C-UCB0599 in addition to a single 360mg oral dose of UCB0599.

Results: There were no severe, serious or drug-related treatment-emergent adverse events. UCB0599 uptake was observed in all white and grey matter regions. Good brain penetration of UCB0599 was observed. The PET outcome measure (11C-UCB0599 volume of distribution) corresponding to total brain:total plasma at equilibrium (range: 0.3 to 0.8) and brain biodistribution appeared to be independent of dose administered. The rate of UCB0599 brain uptake was consistent with rapid free distribution of UCB0599 across the blood-brain-barrier.

Conclusion: Oral UCB0599 was generally well-tolerated and distributed throughout the brain. UCB0599 brain exposure was similar to data obtained in animal models of PD, which were associated with reductions in alpha-synuclein pathology and improved phenotype. Coupled with the data from animal models of PD, these results support the continued development of UCB0599 for the potential to slow the progression of PD.

Disclosure: This study was funded by UCB Pharma.

OPR-104

Phase II PASADENA Part one Week 52 results: Evaluating safety and efficacy of prasinezumab in early Parkinson's disease

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Background and aims: No current treatments slow the progression of Parkinson's disease (PD). The PASADENA study (NCT03100149), a 52-week randomised, double-blind, placebo-controlled study, evaluated the efficacy and safety of intravenous prasinezumab, a monoclonal antibody targeting extracellular alpha-synuclein, in early PD.

Methods: 316 participants were enrolled (diagnosis ≤2 years; Hoehn & Yahr Stages I–II). The primary endpoint was the change in Movement Disorder Society-Unified Parkinson's disease Rating Scale (MDS-UPDRS) Total score from baseline to Week 52. Secondary and exploratory endpoints included: changes in MDS-UPDRS Part III, MDS-UPDRS Part III subscores, other clinical and digital endpoints, and imaging biomarkers.

Results: MDS-UPDRS Total score was -1.30 (-14%; 80% CI: -3.18, 0.58) for pooled doses versus placebo; -2.02 for prasinezumab 1500mg (–20.8%; 80% CI: -4.21, 0.18) and -0.62 for prasinezumab 4500mg (-6.4%; 80% CI: –2.82, 1.58). MDS-UPDRS Part III was -1.44 (-25.0%; 80% CI: -2.83, -0.06) for pooled treatment versus placebo; -1.88 for prasinezumab 1,500mg (-33.8%; 80% CI: -3.49, -0.27) and -1.02 for prasinezumab 4,500mg (-18.3%; 80% CI: -2.64, 0.61). MDS-UPDRS Part III site rating (Figure 1), MDS-UPDRS Part III bradykinesia subscore, digital motor endpoints (Figure 2), and time to worsening of motor symptoms supported this signal. Additional subgroup analyses will also be presented. There were no life-threatening adverse events or immunogenicity concerns.

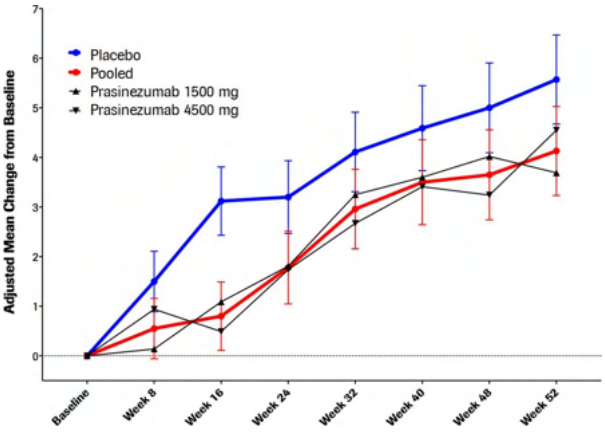

Figure 1. Change in MDS-UPDRS Part III Total Score from baseline at Week 52 (site rating)

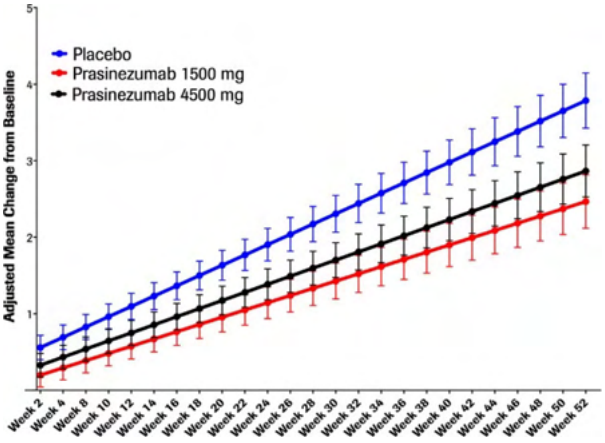

Figure 2. Change in Digital PASADENA Motor Score

Conclusion: Prasinezumab had a favourable safety profile and is the first anti-alpha-synuclein antibody showing efficacy signals on clinical progression of PD motor features, warranting further study.

Disclosure: This study was sponsored by Prothena Biosciences Inc and F. Hoffmann-La Roche Ltd.

OPR-108

Safinamide Improves Non-Motor Symptoms Burden in Parkinson´s Disease: An Open-label Prospective Study

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Background and aims: Some studies observed a benefit of Parkinson´s disease (PD) patients after treatment with safinamide in some non-motor symptoms (NMS). The aim of this study was to analyze the effectiveness of safinamide on NMS burden in PD.

Methods: SAFINONMOTOR (an open-label study of the effectiveness of SAFInamide on NON-MOTOR symptoms in Parkinson´s disease patients) is a prospective open-label single-arm study conducted in five centers from Spain. The primary efficacy outcome was the change from baseline (V1) to the end of the observational period (six months) (V4) in the Non-Motor Symptoms Scale (NMSS) total score.

Results: 50 patients were included between May/2019 and February/2020 (age 68.5±9.12 years; 58% women; 6.4±5.1 years from diagnosis). At six months, 44 patients completed the follow-up (88%). The NMSS total score was reduced by 38.5% (from 97.5±43.7 in V1 to 59.9±35.5 in V4; p<0.0001; table 1 and figure 1). By domains, improvement was observed in sleep/fatigue (-35.8%; p=0.002), mood/apathy (-57.9%; p<0.0001), attention/memory (-23.9%; p=0.026), gastrointestinal symptoms (-33%; p=0.010), urinary symptoms (-28.3%; p=0.003), and pain/miscellaneous (-43%; p<0.0001) (table 1 and figure 2). Quality of life (QoL) also improved with a 29.4% reduction in the PDQ-39SI (from 30.1±17.6 in V1 to 21.2±13.5 in V4; p<0.0001) (table 1 and figure 2). A total of 21 adverse events in 11 patients (22%) were reported, Five of which were severe (not related to safinamide). Dyskinesias and nausea were the most frequent (6%).

Table 1

	V1	N	V4	N	Δ V1-V4	p
NMSS total score	97.48 ± 43.70	50	59.91 ± 35.49	44	-38.5%	**<0.0001**
- Cardiovascular	9.58 ± 2.46	50	6.72 ± 11.94	44	-29.9%	0.268
- Sleep / fatigue	36.08 ± 21.77	50	23.15 ± 18.12	44	-35.8%	**0.003**
- Mood / apathy	34.42 ± 29.89	50	14.49 ± 19.63	44	-57.9%	**<0.0001**
- Perceptual symptoms	4.33 ± 8.67	50	2.84 ± 5.88	44	-34.4%	0.630
- Attention / memory	17.50 ± 17.09	50	13.32 ± 18.19	44	-23.9%	**0.026**
- Gastrointestinal symptoms	19.61 ± 18.01	50	13.13 ± 13.39	44	-33.0%	**0.016**
- Urinary symptos	42.72 ± 30.41	50	30.62 ± 23.94	44	-28.3%	**0.004**
- Sexual dysfunction	28.25 ± 35.69	50	25.28 ± 33.58	44	-10.5%	0.784
- Miscellaneous	33.33 ± 20.73	50	18.99 ± 14.03	44	-43.0%	**<0.0001**
PDQ-39SI	30.07 ± 17.61	49	21.24 ± 13.48	44	-29.4%	**<0.0001**
- Mobility	34.55 ± 27.79	49	29.09 ± 26.85	44	-15.8%	**0.037**
- Activities of daily living	26.50 ± 23.94	49	17.80 ± 17.96	44	-32.8%	**0.014**
- Emotional well-being	44.30 ± 29.34	49	26.33 ± 23.01	44	-40.6%	**<0.0001**
- Stigmatization	15.82 ± 22.79	49	7.67 ± 13.13	44	-51.5%	**0.021**
- Social support	7.48 ± 16.51	49	3.59 ± 12.63	44	-52.0%	0.302
- Cognition	27.17 ± 22.00	49	23.72 ± 22.49	44	-12.7%	0.876
- Communication	20.07 ± 26.73	49	12.12 ± 15.19	44	-39.6%	0.203
- Pain and discomfort	44.56 ± 27.35	49	33.33 ± 19.93	44	-25.2%	**0.018**

Percentage of change in the NMSS total score and the PDQ-39SI and each domain of both scales from V1 (baseline) to V4 (6 months ± 15 days). P values were computed using the Wilcoxon signed-rank test. NMS, Non-motor symptoms; PD, Parkinson´s disease; PDQ-39SI, 39-item Parkinson's Disease Quality of Life Questionnaire Summary Index.

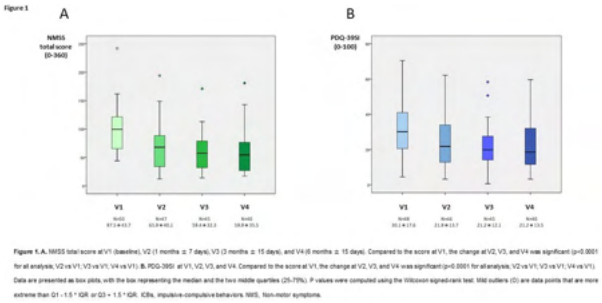

Figure 1.

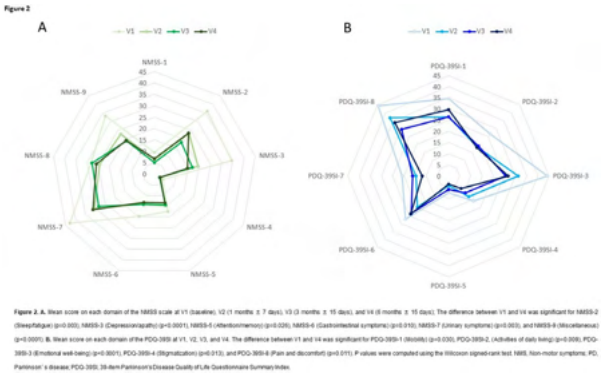

Figure 2.

Conclusion: Safinamide is well tolerated and improves NMS burden and QoL in PD patients at six months.

Disclosure: Nothing to disclose..

OPR-150

Parkinson's disease Symptoms Before and After Levodopa-Carbidopa Intestinal Gel: a Subanalysis From the COSMOS Study

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Background and aims: Patients with Parkinson's disease (PD) initially present with motor and nonmotor symptoms that worsen with progressive disease. There is limited information regarding the response of individual symptoms to levodopa-carbidopa intestinal gel (LCIG) treatment.

Methods: COSMOS (COmedication Study assessing Mono- and cOmbination therapy with levodopa-carbidopa inteStinal gel; NCT03362879) is a retrospective, cross-sectional, multicountry, postmarketing observational study. Patients with advanced PD were evaluated at a single study visit conducted at least 12 months after LCIG initiation and via retrospective record review. This subanalysis assessed changes in PD symptoms following LCIG introduction (improvement/no change vs worsening).

Results: Of 409 total patients, most reported improvement or no change in individual symptoms following LCIG initiation [Table 1]. In general, patients experiencing improvement or no change in symptoms were younger, had shorter disease duration, had greater improvements in "Off" time following LCIG treatment, and had greater improvements in dyskinesia severity following LCIG treatment compared with patients experiencing symptom worsening [Table 2]. Rates of healthcare resource use generally aligned with progression of motor symptoms. Patients with balance problems, freezing of gait, or gait impairment at study visit had the highest rates of resource use [Table 3]. Adverse events were similar to those reported in other LCIG studies.

Table 1. Change in Symptoms Following LCIG Treatment

Motor Symptoms	Improved, n (%)	Not Changed, n (%)	Worsened, n (%)
Tremor	207 (52.5)	156 (39.6)	31 (7.9)
Dystonia/cramps	166 (43.2)	173 (45.1)	45 (11.7)
Gait impairment	183 (46.2)	129 (32.6)	84 (21.2)
Balance problems	151 (38.5)	136 (34.7)	105 (26.8)
Freezing of gait	202 (52.2)	131 (33.9)	54 (14.0)
Dyskinesia	202 (52.6)	105 (27.3)	77 (20.1)
Nonmotor Symptoms			
Anxiety	144 (38.4)	183 (48.8)	48 (12.8)
Pain	142 (37.7)	179 (47.5)	56 (14.9)
Cognitive impairment	50 (12.9)	210 (54.1)	128 (33.0)
Depression	136 (35.1)	173 (44.6)	79 (20.4)
Apathy	66 (18.0)	216 (59.0)	84 (23.0)
Fatigue	143 (40.6)	133 (37.8)	76 (21.6)
Urinary symptoms	107 (29.4)	144 (39.6)	113 (31.0)
Constipation	163 (44.5)	141 (38.5)	62 (16.9)
Orthostatic hypotension	46 (12.3)	265 (71.0)	62 (16.6)
Symptoms Related to Treatment			
Hypersexuality	23 (6.2)	332 (89.0)	18 (4.8)
Compulsive shopping	13 (3.4)	351 (91.9)	18 (4.7)
Gambling	16 (4.2)	361 (94.0)	7 (1.8)
Binge eating	23 (6.0)	340 (88.5)	21 (5.5)
Punding	25 (6.6)	325 (85.3)	31 (8.1)
DDS	22 (5.7)	348 (90.9)	13 (3.4)

Values represent the proportions of patients reporting improvement, no change, or worsening of symptoms from before LCIG initiation to patient visit.
Improved indicates positive changes on prevalence, severity, or frequency.
Not changed indicates that an existing symptom did not change; or that the symptom had not been present and did not develop.
Worsened indicates negative changes on prevalence, severity, or frequency.
DDS, dopamine dysregulation syndrome; LCIG, levodopa-carbidopa intestinal gel.

Table 2. Clinical Characteristics by Change in PD Motor Symptoms

Characteristic	Tremor	Dystonia	Gait Impairment	Balance Problems	Freezing of Gait	Orthostatic Hypotension
	Improved/Not Changed vs. Worsened					
Age at LCIG initiation, years	66.5 67.6 n = 348 n = 29 (*P* = .3103)	66.3 67.6 n = 326 n = 44 (*P* = .2650)	65.9 68.6 n = 296 n = 82 (*P* = .0089)**	66.0 68.1 n = 274 n = 103 (*P* = .0515)	66.1 68.1 n = 317 n = 53 (*P* = .0643)	66.3 68.9 n = 303 n = 59 (*P* = .0308)*
Time from PD diagnosis to LCIG initiation, years	13.0 11.9 n = 349 n = 29 (*P* = .3119)	12.8 13.5 n = 327 n = 44 (*P* = .3223)	12.8 13.0 n = 297 n = 82 (*P* = .3706)	12.6 13.2 n = 275 n = 103 (*P* = .2125)	12.7 13.5 n = 318 n = 53 (*P* = .3026)	12.5 14.7 n = 304 n = 59 (*P* = .0210)*
Change[a] in "Off" time, hours	−4.1 −2.9 n = 252 n = 19 (*P* = .3105)	−4.1 −2.8 n = 241 n = 27 (*P* = .2870)	−4.2 −3.1 n = 221 n = 52 (*P* = .0044)**	−4.2 −3.7 n = 207 n = 65 (*P* = .2271)	−4.2 −2.8 n = 236 n = 34 (*P* = .0255)*	−4.1 −4.1 n = 224 n = 44 (*P* = .5873)
Change[a] in dyskinesia duration, hours	−1.8 −2.1 n = 244 n = 20 (*P* = .9963)	−1.8 −1.7 n = 235 n = 26 (*P* = .6905)	−2.0 −0.9 n = 214 n = 51 (*P* = .0473)*	−1.7 −2.1 n = 200 n = 65 (*P* = .7210)	−1.9 −1.3 n = 232 n = 31 (*P* = .2395)	−1.7 −2.4 n = 215 n = 44 (*P* = .6054)
Change[a] in dyskinesia duration or "Off" time (during waking hours), hours	−6.0 −5.5 n = 235 n = 17 (*P* = .7797)	−6.1 −4.1 n = 227 n = 22 (*P* = .2256)	−6.3 −4.1 n = 207 n = 46 (*P* = .0067)**	−6.0 −5.9 n = 194 n = 59 (*P* = .9165)	−6.2 −4.0 n = 222 n = 29 (*P* = .0171)*	−5.9 −6.5 n = 207 n = 43 (*P* = .3493)
Change[a] in the severity of dyskinesias[b]	−0.9 −0.5 n = 326 n = 30 (*P* = .0581)	−0.9 −0.3 n = 314 n = 39 (*P* = .0078)**	−0.9 −0.6 n = 281 n = 79 (*P* = .0598)	−0.9 −0.7 n = 257 n = 99 (*P* = .4259)	−0.9 −0.4 n = 304 n = 47 (*P* = .0153)*	−0.9 −0.7 n = 284 n = 60 (*P* = .2414)

Values represent means for patients experiencing improvement or no change vs worsening in individual motor symptoms (tremor, dystonia, gait impairment, balance problems, freezing of gait, or orthostatic hypotension).
Asterisks indicate statistical significance between patients with symptoms that improved or had no change vs patients with symptoms that worsened; *P* < .05 (*) and *P* < .01 (**).
[a]Change is measured from before LCIG treatment to study visit.
[b]Calculated as the weighted average of the change in the proportion of patients with dyskinesia from before LCIG initiation to patient visit.
LCIG, levodopa-carbidopa intestinal gel; PD, Parkinson's disease.

Table 3. Percentage of Patients that Use Healthcare Resources by Symptom Presence at Patient Visit

Healthcare Resource Use, %	Tremor	Dystonia	Gait Impairment	Balance Problems	Freezing of Gait	Orthostatic Hypotension
Primary occupancy						
Retired due to PD[a]	16	17	35	31	28	13
Sick leave due to PD[b]	0	33	50	33	17	33
Living situation[c]						
Permanent living in a nursing/home institution	25	25	81	63	63	31
Help in ADL	37	33	76	70	51	31
Problems before starting LCIG[c]						
Forgetting to take the pill	36	41	77	72	54	36
Dosage or medication error	34	42	78	71	49	38
Problems swallowing the pill	52	57	83	83	63	28
Help to remember to take the medication[c]	35	40	79	73	54	37
Physician-visit hospitalisation[c]						
Scheduled visits to physician	36	41	68	64	57	29
Extra visits to physician	36	44	63	63	50	31
Emergency room visits	52	48	91	83	61	37
Hospitalisation	43	51	80	80	56	27
Admissions due to PD	43	46	78	76	57	24
Frequency of visits[d]						
General practitioner (increased vs reduced[e])	8 vs 21	9 vs 23	8 vs 23	8 vs 23	7 vs 19	6 vs 27
Nurse (increased vs reduced[e])	16 vs 8	13 vs 8	18 vs 9	17 vs 8	14 vs 7	23 vs 10

[a]Based on the total number of retired patients, regardless of symptoms or reasons for retirement.
[b]Based on the total number of patients on sick leave, regardless of symptoms or reasons for sick leave.
[c]Based on the total number of patients using a given healthcare resource, regardless of symptom.
[d]Based on the total number of patients reporting a given symptom at study visit.
[e]Compared to before LCIG initiation.
ADL, activities of daily living; LCIG, levodopa-carbidopa intestinal gel.

Conclusion: Following more than 12 months of LCIG treatment, most patients experienced improvement or no change in symptoms, despite the natural progression of the disease. Treatment with LCIG may help control symptoms that impact healthcare resource use.

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Ageing and Dementia 2

OPR-121

Promising diagnostic accuracy of Plasma GFAP within the AD continuum

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Background and aims: Due to the increasing number of patients suffering from Alzheimer's disease (AD), recent studies have been looking for a possibility to establish fluid biomarkers with conventional blood analysis. A promising biomarker for tracking neurodegeneration could be Glial Fibrillary Acidic Protein (GFAP), an intermediate filament protein of astrocytes. Analysis of GFAP in blood has shown an increase in patients with AD in comparison to healthy controls. The aim of this study was to examine the utility of GFAP as a possible biomarker along the AD continuum.
Methods: We included a total of 185 Patients, 141 Patients with a diagnosis along the clinical spectrum of AD, i.e. Subjective Cognitive Decline (SCD, n=18), Mild Cognitive Impairment (MCI, n=63), AD (n=60), and additionally 44 age-matched healthy controls (HC) with no sign of neurodegenerative disorder or cognitive decline. Concentrations of GFAP in Plasma and CSF were quantified using ultrasensitive single molecule array (SIMOA).
Results: Median Concentration of GFAP in plasma was 79pg/ml in HC, 111 pg/ml in SCD, 167.5pg/ml in MCI and 181.9pg/ml in AD. We observed a good diagnostic discrimination between HC, MCI and AD groups ($p<0.001$). Interestingly, analysis of GFAP in plasma could further distinguish between groups with SCD and AD ($p=0.01$).
Conclusion: Analysis of GFAP in plasma has shown a good diagnostic accuracy in differentiating patients with AD from healthy controls. Furthermore, this biomarker could aid in a better distinction of patients in different predementia stages and potentially give more information about disease progression than already established AD biomarkers.
Disclosure: Nothing to disclose.

OPR-122

Plasma Neurofilaments, Semantic Verbal Fluency and Clock Drawing Test may detect Alzheimer's disease Fast Decliners

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Background and aims: Alzheimer's disease (AD) is characterized by a heterogeneous course. Predicting a fast rather than a slow decline over time is crucial to provide a reliable prognosis and to elaborate stricter enrolment criteria in clinical trials. We aimed at identifying progression rate predictors to assess already at baseline the risk to fast progress
Methods: 65 AD subjects were included. At baseline, CSF AD biomarkers, neuropsychological assessment and plasma neurofilaments (NfL) concentrations were available. Magnetic Resonance Imaging (MRI) based adjustment for hippocampal volume and vascular burden was available in a sub-sample of 27 patients. Patients were labelled FAST or SLOW depending on the Mini Mental State Test (MMSE) points lost per year (FAST if more than three points). We adopted Receiver Operating Characteristics (ROC) curves and Linear Regression Models to assess the risk to fast decline
Results: At baseline no differences were found between FAST and SLOW subgroups in demographics, CSF AD biomarkers' concentrations and MMSE scores. FAST decliners had higher plasma NfL concentrations and performed worse at two neuropsychological tests: Semantic Verbal Fluency (SVF) and Clock Drawing Test (CDT). After adjustment for MRI parameters, CDT kept a trend towards significance ($p=0.056$). The risk to FAST decline over time was 4% if no predictor was abnormal and 79% if all the three predictors were abnormal
Conclusion: An easily applicable algorithm including plasma neurofilament measurement and two neuropsychological tests that are worldwide adopted in clinical practice (SVF and CDT) may allow the clinicians to reliably assess the risk to fast decline already at baseline
Disclosure: Nothing to disclose

OPR-123

Time in the salience network predicts conversion in presymptomatic mutation carriers in familial frontotemporal dementia

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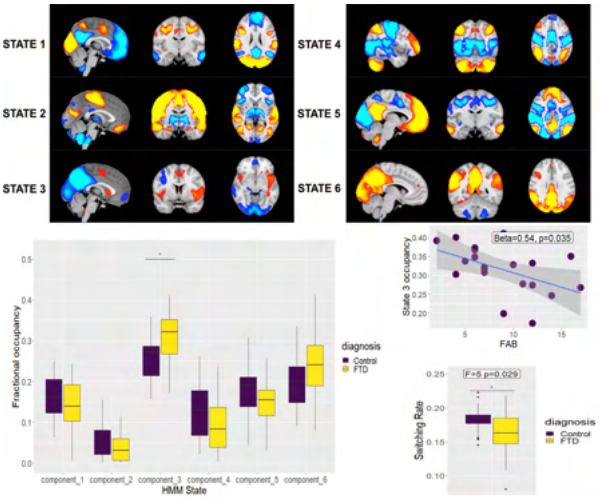
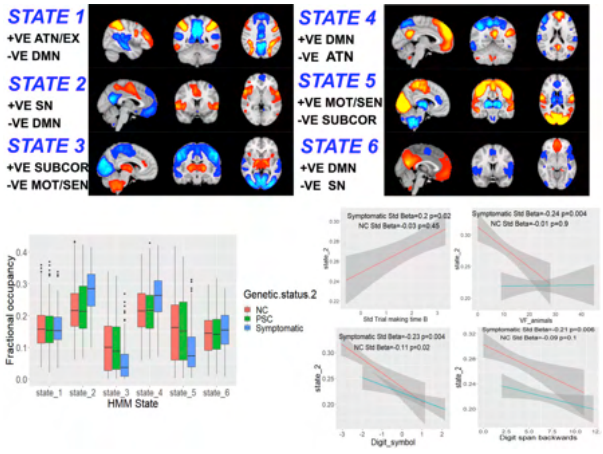
Background and aims: Familial frontotemporal dementia (FTD) is characterised by a long presymptomatic prodrome followed conversion to symptomatic disease. There is a pressing need to understand the underlying pathophysiology caused by FTD mutations, and their relationship to clinical symptoms. Neurotransmitter changes, network topology and clinical phenotypes suggest that connectivity changes in FTD are dynamic.

Methods: For hypothesis generation, 38 participants with sporadic behavioural variant frontotemporal dementia and 30 healthy controls were recruited from Cambridge University. For hypothesis testing, 150 symptomatic FTD mutation carriers, 320 presymptomatic mutation carriers and 309 family members without mutations were included from the longitudinal multinational Genetic FTD Initiative (GENFI). They underwent clinical and neuropsychological testing and resting-state functional MRI. Dynamic connectivity was quantified by hidden Markov models, excluding participants with supra-threshold motion parameters. Key metrics of dynamic connectivity (switching rates, fractional occupancy), focussed on the salience network.

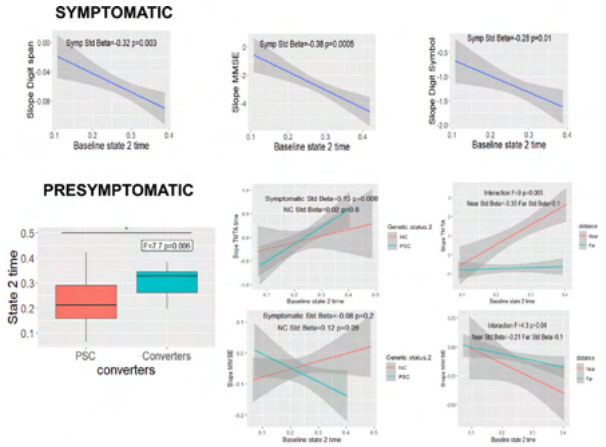
Results: In both cohorts, FTD increased the proportion of time spent with activation of the salience network, and components of the default mode network. In symptomatic participants, salience network occupancy correlated with neuropsychological impairment. In mutation carriers, salience network occupancy were related to age and Expected Years until Onset. In presymptomatic mutation carriers occupancy differed between those who subsequently converted to the symptomatic phase within two years. Baseline salience network occupancy predicted subsequent decline in neuropsychological function.



Mean activation maps for the six hidden Markov model states from Cambridge. Participants with frontotemporal dementia had increased time in state 3 (salience; F=7.8, corrected p=0.042), and time in this state correlated with the Frontal Assessment Battery.



Dynamic connectivity in GENFI. Symptomatic participants had increased time in states predominantly representing salience network, correlating with neuropsychological assessment (symptomatic participants in red, non-carriers in blue).



Longitudinal GENFI analysis. Baseline salience occupancy predicts a) further cognitive decline in symptomatic patients, b) age-related decline in the presymptomatic phase and c) differed between converters and other presymptomatic mutation carriers

Conclusion: Dynamic network abnormalities in frontotemporal dementia predict cognitive decline and conversion to symptomatic disease

Disclosure: All authors have no disclosures relevant to this study

OPR-124

Interleukin 1B in Multiple Sclerosis: analysis of a polymorphism in the gene promoter region

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Background and aims: Increased IL-1B expression in and around multiple sclerosis (MS) lesions has been reported. The rs16944 (-511C>T) polymorphism, known to increase IL-1B expression, has been studied in MS populations, with inconsistent results. Our aim is to assess the role of rs16944 polymorphism in MS susceptibility and clinical outcome in a Portuguese cohort.

Methods: rs16944 polymorphism was genotyped in a cohort of 599 patients with a definitive MS diagnosis and 237 ethnically matched healthy controls. Demographic and clinical data, including the Expanded Disability Severity Score (EDSS), Multiple Sclerosis Severity Scale (MSSS) and Age-Related Multiple Sclerosis Severity (ARMSS), were reviewed. Statistical analyses were performed using SPSS (v26).

Results: No statistically significant differences were observed comparing genotypic frequencies between MS patients (47.1% CC, 42.1% CT, 10.8% TT) and controls (45.6% CC, 46.8% CT, 7.6% TT). We did not observe statistically significant differences according to HLA-DRB1*15, gender, MS course or disease modifying treatment. The presence of the rs16944T allele may predispose to a better clinical outcome measured by EDSS and ARMSS (EDSS: CC=4±2.5; CT+TT=3.5±2.5 p=0.041; ARMSS: CC=4.93±2.92; CT+TT=4.44±2.82, p=0.037).

Conclusion: The rs16944 (-511C>T) polymorphism may have a role on the MS clinical outcome. Further studies of the genetic and epigenetic mechanisms regulating IL-1B pathway are needed to clarify the link between this polymorphism and disease severity.

Disclosure: Nothing to disclose.

OPR-125

Benefit of albumin replacement to treat functional impairment in alzheimer's is robust to common sources of confounding

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Background and aims: The Alzheimer's Management By Albumin Replacement (AMBAR) study examined treatment effects over 14-months on the Alzheimer's disease Cooperative Study – Activities of Daily Living (ADCS-ADL), one of two AMBAR primary endpoints. AMBAR-treated patients with MMSE scores ranging from 18 to 26 had significantly less decline in ADCS-ADLs than placebo patients (Boada et al., 2020). This research presents sensitivity analyses on testing robustness of clinical trial and HEOR modeling assumptions.
Methods: AMBAR study details are reported elsewhere (Boada et al., 2020). In this analysis, three active treatment arms were pooled and compared to the placebo arm. Treatment response, defined as the difference in ADCS-ADL from the baseline to the final visit at month 14, was adjusted for patient level missing data (pattern-mixtures) and multiplicity in three sensitivity analyses.
Results: The analysis sample included 169 individuals receiving active treatment and 64 on placebo. The sample had a mean age of 69 years and was 54% female. A total of 70.5% of the sample completed all study visits. Among the 29.5% missing at least one visit, the majority (n=26, 8.1%), were lost to follow-up. Adjusted p-values obtained from the sensitivity analyses ranged from 0.0439, to 0.0491, to 0.0490), indicating sustained robust significance.
Conclusion: The previously reported functional benefits of AMBAR treatment on ADCS-ADL remained robust after sensitivity analyses adjusting for missing data and multiple comparisons.
Disclosure: This study was funded by Grifols SSNA a maker of Albutein®

OPR-126

Association of blood pressure, its treatment and treatment efficacy with white matter lesions in the 1000BRAINS study

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Background and aims: White matter lesions (WMLs) are a frequent finding in cerebral MRI scans of older people. Since vascular risk factors, especially hypertension, are associated with small vessel disease, offering a potential for preventive strategies, we analysed the association of blood pressure (BP), its treatment and treatment efficacy with WML volume in the population-based 1000BRAINs study.
Methods: In 560 participants of the 1000BRAINS study (65.2±7.5 years, 51.4% males), we analysed the association of systolic blood pressure (SBP), diastolic blood pressure (DBP) and antihypertensive medications with WML volume in univariable and multivariable linear regression models adjusting for confounding variables. Further, we analysed treatment efficacy using a classification of six BP treatment groups defined by antihypertensive medication and level of BP: 1) untreated BP <120/<80mmHg, 2) untreated SBP 120–139mmHg or DBP 80-89mmHg, 3) untreated BP 140/90mmHg, 4) treated BP <120/<80mm Hg, 5) treated SBP 120-139mmHg or DBP 80-89mmHg, 6) treated BP 140/90mmHg.
Results: In multivariable regression models adjusting for age, sex, education, depression, alcohol consumption and smoking, continuous SBP (B=0.63 per 10mmHg, 95%CI=0.32–0.94), DBP (0.64, 0.37–0.91) and antihypertensive treatment (1.23, 0.14–2.23) were significantly associated with WML volume (in cm3). Regarding treatment efficacy, only participants with hypertension despite treatment (treated BP 140/90mmHg) had significantly increased WML volume (4.24, 2.36–6.13) compared with normotension without treatment (untreated BP <120/<80mmHg).
Conclusion: Our results suggest, that WMLs represent a marker of advanced hypertension pathology, calling for early markers of brain damage such as structural and functional connectivity.
Disclosure: Nothing to disclose.

OPR-194

Genotype-phenotype data of PSEN1 p. CYS263PHE carriers in Belgian-Flanders Alzheimer's disease patients

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Background and aims: We identified 13 unrelated index patients carrying the presenilin 1 (PSEN1) missense mutation, p.Cys263Phe in an Alzheimer's disease (AD) patient's cohort of Flanders Belgian. In DR1633 family three affected relatives were identified (n=17). We aimed to delineate a clinicopathological phenotype compared to genotype–phenotype data of AD patients carrying other causal mutations i.e. PSEN1 (n=25), PSEN2 (n=1), and APP (n=5).

Methods: Reviewing medical records of mutation carriers to obtain clinicopathological data for defining genotype-phenotype data.

Results: Mean onset age of Cys263Phe carriers was 63.6±5.9 years (range 53–74), with a disease duration of 9.0±4.0 years (range 4–13). A positive familial history was present in 92.9% of the carriers and autosomal dominant co-segregation of AD in family DR1633. Amnestic presentation was present in all carriers, however five (38.5%) patients also showed significant frontal symptoms. OS1004 Neuroimaging (n=12) displayed diffuse (sub) cortical atrophy, with evident hippocampal atrophy in three carriers. We observed severe signs of small vessel disease in five patients. Cerebrospinal fluid AD biomarkers were characteristic for AD in all.

Neuropathology in two patients demonstrated severe levels of AD hallmarks plus severe signs of cerebral amyloid angiopathy (CAA). Carriers of p.Cys263Phe had a later age at onset (63.6 years) than other PSEN1 carriers (50.8 years) or other causal gene mutation carriers (51.1 years).

Conclusion: PSEN1 p.Cys263Phe carriers present with early-onset AD. Severe levels of AD neuropathology were seen with high levels of CAA. Disease onset of p.Cys263Phe carriers was later than other causal gene mutation carriers.

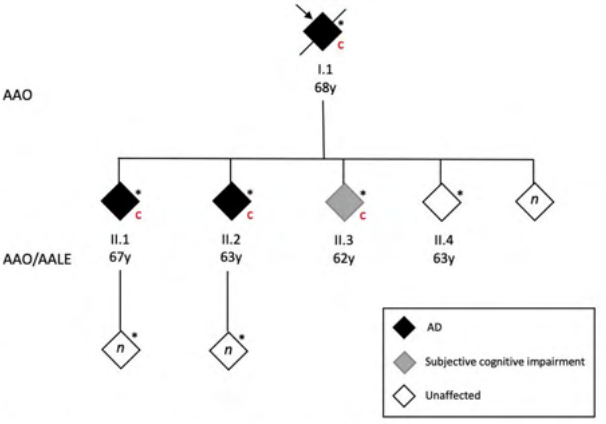

Figure 1. Pedigree DR1633 To protect the privacy of the family members, the gender of each person was masked, the order of sibs was scrambled and the number (n) of tested at-risk individuals shown in white diamonds was not specified. Filled symbols are clinically affected patients with their age at onset (AAO) or age at last examination (AALE) in years (y) below the symbol. An asterisk identifies the family members of whom genomic DNA was available and a 'c' identifies the *PSEN1* p.Cys263Phe mutation carriers. The arrow identifies the proband of the family. Only the clinically affected patients known to carry the mutation and of whom clinical records were available, were described in this paper. Other family members pictured as clinically affected were not described because the clinically affected state was only based on oral information obtained from relatives or because their mutation status was not known.

Pedigree DR1633

Disclosure: Nothing to disclose

Monday, June 21 2021
Epilepsy: Anti-seizure medications, surgery, and outcomes

OPR-060

Temporal Lobe Resection Reorganizes Language Networks in Patients with Epilepsy

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Background and aims: Anterior temporal lobe resection (ATLR) can control seizures in patients with intractable temporal lobe epilepsy (TLE) but may impair language function. We used functional magnetic resonance imaging (fMRI) to study changes of the functional language connectome in left-hemisphere dominant patients after left or right ATLR.
Methods: We studied 44 patients with unilateral medial TLE due to hippocampal sclerosis (24 left) and 18 healthy controls on a three Tesla MRI scanner. All subjects performed language fMRI (verbal fluency) and neuropsychological testing (verbal fluency, naming) preoperatively, and again four months after ATLR. Connectome analysis was based on 50 cortical language-related and four hippocampal regions of interest (ROIs). Network-based statistics was used to analyse network changes between pre- and postoperative data for left and right TLE individually.
Results: For both left and right TLE, a significantly reduced connectivity structure ($p<0.0001$) was observed after ATLR. Left TLE showed primarily impaired connectivity for the left and right inferior frontal cortex (IFC) and both temporal lobes, while right TLE showed alterations particularly for the right IFC. Left TLE showed increased fronto-temporal connectivity within left and right hemisphere, and within the right IFC. Right TLE showed a widespread increase in connectivity especially for the right IFC to ipsi- and contra-lateral regions.
Conclusion: Widespread disruptions of the language connectome primarily in left TLE emphasized the critical role of the left hippocampus during language tasks, and post-operative reorganization provided evidence of multiple systems supporting language function.
Disclosure: Nothing to disclose.

OPR-152

Deep brain stimulation of the ANT for drug resistant epilepsy in a real-world setting: MORE registry 2-year results

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Background and aims: The efficacy of deep brain stimulation (DBS) of the anterior nucleus of the thalamus (ANT) in drug resistant epilepsy (DRE) patients was demonstrated in the double-blind Stimulation of the Anterior Nucleus of the Thalamus for Epilepsy (SANTE) randomized controlled trial. The Medtronic Registry for Epilepsy (MORE) aims to understand the safety and longer-term effectiveness of ANT-DBS therapy in routine clinical practice.
Methods: MORE is an observational registry collecting prospective and retrospective clinical data. Participants were at least 18 years old, with focal DRE recruited across 25 sites from 13 countries. They were followed for at least two years in terms of seizure frequency (SF), health-related quality of life (Quality of Life in Epilepsy Inventory 31 (QOLIE-31), depression, and safety outcomes. Outcomes in the complete case population at two years are reported.
Results: Of the 191 patients recruited, 170 (mean age of 35.6 years, 43% female) were analysed. At entry, 38% of patients reported cognitive impairment. Over two years the median monthly SF decreased progressively by 33,1% (p-value<0.0001) and QOLIE-31 improved by a median 2-point. No change in depression severity was seen. Factors influencing SF reduction included seizure type, absence of cognitive impairment and site implant volume. The most reported adverse events were new or worsening seizures (16% of patients), memory impairment (15%) and depression (13%).
Conclusion: The MORE registry supports the benefit and safety of ANT-DBS therapy in a real-world setting in the 2-years following implantation. Patients without cognitive impairment may benefit more from this type of neuromodulation therapy.
Disclosure: This study was sponsored by Medtronic plc

OPR-153

Safety of adjunctive cenobamate in adults with uncontrolled focal seizures: time to onset, duration, and severity of AEs

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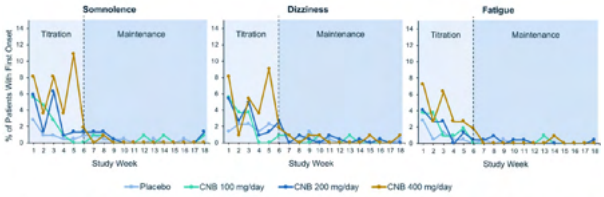
Background and aims: Cenobamate is a new antiseizure medication (ASM) approved in the US for uncontrolled partial-onset (focal) seizures in adults. Two international, double-blind, placebo-controlled trials with open-label extensions (OLEs; C013/C017) and a large international open-label safety study (C021) demonstrated efficacy and safety. Here we characterize the most common adverse events (AEs) in these studies.

Methods: Adults with uncontrolled focal seizures and taking 1-3 concomitant ASMs were enrolled (C013/C017/C021). Concomitant ASM changes were not allowed during the double-blind period (DB) but were allowed during OLEs (C013/C017) and for most C021 patients. C021 cenobamate titration started lower and up-titrated slower than C013/C017. Time of 1st onset (pooled C013/C017 DB and OLEs; C021), duration of all AE occurrences (pooled C013/C017 DB), and severity (pooled C013/C017 DB; C021 first 18 weeks) of somnolence, dizziness, and fatigue were examined.

Results: First onset of the most common AEs emerged throughout the DB (Figure 1) and OLE (Figure 2), mostly during titration. In C021 the peak occurred when dosing reached 50 mg/day (Figure 2). Median duration in days (DB, all occurrences) was: somnolence 32 cenobamate versus 22 placebo, dizziness 11 cenobamate versus eight placebo, and fatigue 34 cenobamate versus 20.5 placebo. AEs in the DB were primarily mild or moderate, with few severe AEs (Figure 3). In C021, more patients reported mild AEs and fewer reported moderate and severe AEs.

Conclusion: Onset of the most common AEs occurred primarily during titration; AEs were generally self-limited in duration and were mainly mild or moderate in severity. Slower titration reduced the severity of AEs.

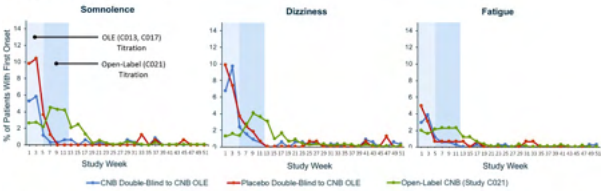
Figure 1. Time of first onset of somnolence, dizziness, and fatigue during the double-blind period (pooled C013 and C017).



C013 titration: starting dose 50 mg/day, increased 50 mg/week every 2 weeks to 200 mg/day target. Amended C017 titration: starting dose 50 mg/day, increased 50 mg/week until target of 100 or 200 mg/day reached; once 200 mg/day reached, dose was increased by 100 mg/day per week to target dose 400 mg/day. Prior to amendment, 46/437 patients (10.5%) received a starting dose of 100 mg/day, increased 100 mg/week to target. CNB, cenobamate.

Figure 1.

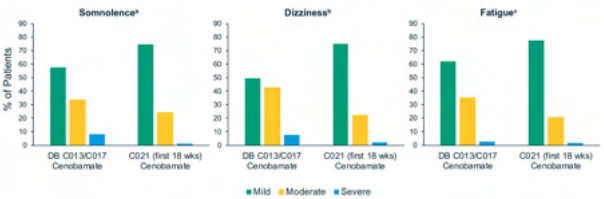
Figure 2. Time of first onset of somnolence, dizziness, and fatigue during the OLE (pooled C013 and C017) and the open-label safety study (C021).



C013 OLE titration: initial 100 mg/day dose increased by 50 mg/week every 2 weeks to 200 mg/day; further increases up to 400 mg/day allowed. C017 OLE titration: 2-week conversion to the target dose of 300 mg/day. C021 titration: initial 12.5 mg/day (2 weeks) increased to 25 mg/day (2 weeks), 50 mg/day (2 weeks), then increased by 50 mg/day every 2 week to 200 mg/day. Further biweekly increases by 50 mg/day allowed up to 400 mg/day. CNB, cenobamate; OLE, open-label extension.

Figure 2.

Figure 3. Among patients experiencing AEs, the percentage reporting mild, moderate, and severe.



[a]Total patients reporting somnolence in DB was 109/442 (24.7%) and in C021 was 356/1340 (26.6%). [b]Total patients reporting dizziness in DB was 103/442 (23.3%) and in C021 was 275/1340 (20.5%). [c]Total patients reporting fatigue in DB was 71/442 (16.1%) and in C021 was 210/1340 (15.7%). AEs, adverse events; DB, double-blind period.

Figure 3.

Disclosure: Studies C013 (NCT01397968), C017 (NCT01866111), and C021 (NCT02535091) were sponsored by SK Life Science, Inc. (Paramus, NJ, USA) and these analyses were supported by Arvelle Therapeutics International GmbH (Zug, Switzerland).

OPR-186

Vanishing of multidien cycles with seizure freedom in focal epilepsy

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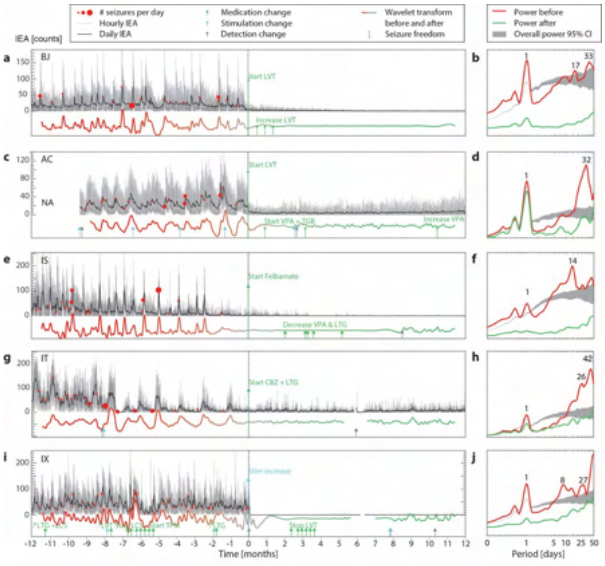
Background and aims: In refractory focal epilepsy, cycles of epileptic brain activity organize seizures over multi-day (multidien) timescales, but whether variation in these cycles influences clinical outcome is unknown.

Methods: We identified patients from the RNS System clinical trials (implanted with an intracranial brain stimulator for detecting and treating seizures) who self-reported seizure freedom for at least 12 months. Wherever continuous chronic recordings of EEG features (cEEG) were available, we characterized multidien cycles of interictal epileptiform activity (IEA) using a wavelet transform and compared power spectra before and after clinical seizure freedom. We tested significant peak periodicity against surrogate time series (random permutation of 100 calendar days and their corresponding 24-hour IEA).

Results: 25 out of 256 participants (9.8%) had cEEG available for at least 24 continuous months, the last 12 months without reported seizures. In 15 of them (60%) abrupt seizure freedom coincided with an identifiable treatment change (Fig. 1 a, c, g, e, i), while the rest had a progressive decrease in seizure frequency culminating in seizure freedom. While still having seizures 20 of these 25 participants (80%) had multidien cycles of IEA. Upon becoming seizure free, the magnitude of these cycles strongly decreased in 13 out of 20 subjects (65%) (Fig 1 b, d ,f, h, j).



IEA counts (left) and power spectra (right) for five individuals who reported seizure freedom for at least 12 months following therapy adaptation. During seizure freedom multidien cycles of IEA are strongly reduced (green) compared to the period before (red)

Conclusion: In this cohort, clinical seizure freedom was consistently associated with a decrease in magnitude of multidien IEA cycles, often vanishing completely. Although causal relationships cannot be established, this suggests that multidien IEA cycles may represent novel biomarkers for seizure recurrence over long periods (months to years).

Disclosure: MOB is an employee of the Wyss Center and has a patent pending for Neural Interface System. VRR has been consultant for NeuroPace, Inc. (NP), but declares no funding for this study. TKT/TS are NP employees and declare equity stock options.

Multiple Sclerosis: Therapy: outcome measures

OPR-155

Structural and functional connectivity of the amygdala explain social cognition performances in multiple sclerosis

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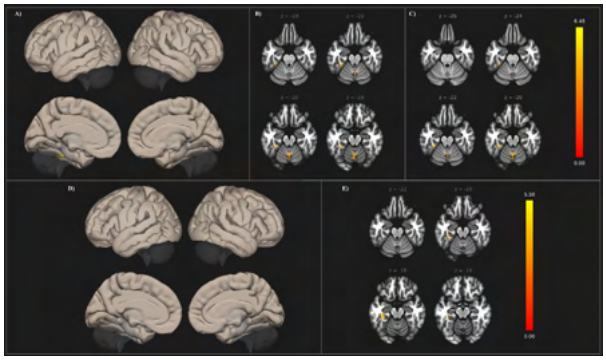
Background and aims: Social cognition (SC) can be impaired in multiple sclerosis (MS) with theory of mind (ToM) as the main domain affected in MS. Amygdala has been shown to be a key structure in modulating social behaviors.
Methods: We prospectively recruited 20 RRMS patients and 15 healthy controls. SC was assessed with the Faux Pas test and a false belief task to evaluate ToM. All participants underwent extensive neuropsychological assessment in addition to the MRI protocol evaluating amygdala-based structural connectivity, using diffusion weighted imaging, and functional connectivity (FC), using both resting-state fMRI and a task-based paradigm consisting of the Reading the Mind in the Eyes Test.
Results: SC and classical cognitive performances of patients did not differ from those of controls. Amygdala was not altered in patients in terms of volume, fractional anisotropy and mean diffusivity (MD). Resting-state FC between the left amygdala and the left frontal pole and paracingulate gyrus was decreased in patients compared to controls ($p < 0.001$) and was associated to the ratio of right answers during the mental task ($r=0.42$; $p<0.05$). As for the mental paradigm, patients showed increased FC between amygdala and temporal and infratentorial regions ($p<0.05$; Figure1), associated to a significant increase in MD of the related tracts ($r=0.74$; $p<0.001$).



Differences between groups (multiple sclerosis > controls) in regional brain responses for the mental task. Color bar represents t-statistics. The z coordinates are in the MNI (Montreal Neurological Institute) space.

Conclusion: The current study supported the importance of amygdala-dependent pathways in the regulation of social behaviors in MS patients. Our population demonstrated preserved SC despite the presence of structural damage. We showed that specific functional reorganization at this stage could represent a beneficial response to structural injury.
Disclosure: Authors have nothing to disclose in relation to the current work.

OPR-156

Symptom severity in neuromyelitis optica spectrum disorder: psychometric properties of the SymptoMScreen questionnaire

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Background and aims: The assessment of self-reported outcomes in neuromyelitis optica spectrum disorder (NMOSD) is limited by the lack of disease-specific measures. The SymptoMScreen (SMSS) is a validated, patient-reported questionnaire for measuring symptom severity in key neurologic domains affected by MS, but has not been thoroughly evaluated in NMOSD. The aim of this study was to assess the dimensional structure and item distributions of the SMSS in a sample of patients with NMOSD.

Methods: A non-interventional, cross-sectional study in adult subjects with NMOSD (Wingerchuk 2015 criteria) was conducted at 13 neuro-immunology clinics across Spain. A non-parametric item response theory procedure, Mokken analysis, was performed to assess the underlying dimensional structure and scalability of items and overall questionnaire. All analyses were performed with JASP (v 0.14.1) and R (v 4.0.3) using the mokken library.

Results: A total of 70 patients were studied (mean age= 47.4 years±14.9, 81.7% female, mean time since diagnosis= 6.1 years±3.9). Symptom severity was low (median SMSS score=19.0 [interquartile range 10.0, 32.0]). The SMSS showed excellent internal reliability (Cronbach's alpha 0.90 [95% CI 0.86, 0.93]) and behaved as a unidimensional scale with all items displaying scalability coefficients (Hi) >0.30. The overall SMSS scalability was 0.45 conforming to a medium scale according to Mokken's criteria. Fatigue (Hi=0.53) and pain (Hi=0.52) were the domains with the highest impact.

Conclusion: The SMSS shows appropriate psychometric characteristics and may constitute a valuable and easy-to-implement addition to measure symptom severity in patients with NMOSD.

Disclosure: This study was funded by the Medical Department of Roche Farma Spain (ML41397). D.P., R.G-B. and J.M. are employees of Roche Farma Spain. None of the other authors report any conflict of interest.

OPR-157

A Functional Composite Endpoint to Characterize Disease Progression in Patients with Active or Non-active SPMS

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Background and aims: Composite endpoints (CEPs) capture disease progression more comprehensively as they account for functions not, or not optimally, captured by Expanded Disability Status Scale (EDSS) alone. A previous analysis, combining SDMT and EDSS, demonstrated high sensitivity in determining treatment effects. Here, 9-Hole Peg Test (9HPT) and Timed 25-Foot Walk Test (T25FWT) are included with SDMT and EDSS in the construction of CEPs. By exploring novel CEPs more relevant to secondary progressive multiple sclerosis (SPMS), we may be able to better characterize progressive disease including differences in active and non-active SPMS.

Methods: In this post hoc analysis, two definitions for time to 6-month confirmed disease progression (6mCDP) were applied for all SPMS patients participating in the EXPAND Core study and in subgroups with active and non-active disease: CEP1 based on EDSS (1-point/0.5-point worsening from baseline of 5/>5, respectively), or 4-points worsening on SDMT, or 20% increase in 9HPT; and CEP2 that in addition to CEP1 included the component of 20% increase in T25FWT (only for patients with baseline EDSS 5.5, since T25FWT was unstable in patients with higher baseline EDSS in the EXPAND study).

Results: Risk reductions of 6m-CDP in the overall, active and non-active SPMS patients assessed by EDSS alone, CEP1 and CEP2 are presented in the table.

Table: 6m-CDP risk reductions based on EDSS alone,ds CEP1 and CEP2

Parameters	6m-CDP risk reduction (%)	HR ratio (95% CI)	P-value
EDSS			
Overall population (siponimod [n=1099], placebo [n=546])	26%	0.74 (0.60; 0.92)	p=0.006
• Active group (siponimod [n=516], placebo [n=263])	37%	0.64 (0.47; 0.87)	p=0.004
• Non-active group (siponimod [n=557], placebo [n=270])	13%	0.87 (0.64; 1.19)	p=0.376
CEP1: EDSS/SDMT/ 9-HPT			
Overall population (siponimod [n=1099], placebo [n=546])	27%	0.73 (0.62; 0.86)	p<0.001
• Active group (siponimod [n=516], placebo [n=263])	30%	0.70 (0.55; 0.88)	p=0.003
• Non-active group (siponimod [n=557], placebo [n=270])	21%	0.80 (0.63; 1.01)	p=0.061
CEP2: EDSS/SDMT/ 9-HPT/T25FWT			
Overall population (siponimod [n=1099], placebo [n=546])	25%	0.75 (0.64; 0.88)	p<0.001
• Active group (siponimod [n=516], placebo [n=263])	29%	0.71 (0.57; 0.89)	p=0.003
• Non-active group (siponimod [n=557], placebo [n=270])	19%	0.81 (0.64; 1.02)	p=0.070

Cox proportional hazards model was used for detection of treatment effects on EDSS alone, CEP1 and CEP2.
6m-CDP, 6-month confirmed disease progression; 9-HPT, 9-Hole Peg Test; CEP, composite endpoints; EDSS, Expanded Disability Status Scale; HR, hazard ratio; SDMT, Symbol Digital Modalities Test; T25FWT, Timed 25-Foot Walk Test

Conclusion: Adding SDMT and 9HPT to the EDSS assessment (CEP1) allows detection of treatment effects on a broader spectrum of symptoms in SPMS compared with EDSS alone, including in patients with non-active disease. Addition of T25FWT in CEP2 did not increase precision of HR ratio estimates.

Disclosure: The study was supported by Novartis Pharma AG, Switzerland. The detailed author disclosures will be presented in the subsequent presentation.

OPR-158

Association Between Brain Volume and Clinical/Patient-Reported Outcome Measures for Patients With Multiple Sclerosis

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Background and aims: Brain volume loss is an important attribute to multiple sclerosis (MS) patients. We estimated the association between brain volume and clinical/patient-reported outcomes in MS.
Methods: Data from the Comprehensive Longitudinal Investigation of MS at Brigham and Women's Hospital (CLIMB) were included in this retrospective analysis. Eligible patients had two MRI scans 24 months apart with corresponding clinical visits with Expanded Disability Status Scale (EDSS) scores. Whole brain volume was determined from MRI at baseline and month 24. Data also included the following outcome measures for a subset of patients: mental component summary (MCS) and physical component summary scores from the Medical Outcomes Short-Form Health Survey, Modified Fatigue Impact Scale, Center for Epidemiologic Studies-Depression Scale (CES-D), and Symbol Digit Modalities Test. The association between baseline brain volume and 24-month change in brain volume with each outcome measure at baseline, months 24 and 60 was estimated using linear regression adjusting for age, sex, and disease duration.
Results: Baseline whole brain volume was associated with baseline MCS, CES-D, and EDSS ($p<0.05$ each comparison) and with month 60 CES-D and EDSS ($p<0.05$ each comparison); 24-month change was associated with month 60 CES-D ($p=0.04$). No significant associations were observed between 24-month change in brain volume and change in outcome measures.
Conclusion: Whole brain volume was associated with concurrent and month 60 EDSS and CES-D and was a stronger predictor of clinical/patient-reported outcomes. While 24-month change in brain volume was associated with CES-D, longer follow-up may be required to identify association with other outcome measures.
Disclosure: BH, BIG, TC, and HW: Employment – Brigham and Women's Hospital ES and KH: Employment – Analysis Group DS, TP, KG: Employment – Bristol Myers Squibb

Multiple Sclerosis: Neuromyelitis Optica Spectrum Disorder (NMOSD)

OPR-159

MR T2-relaxation time as an indirect measure of brain water content and disease activity in NMOSD

L. Cacciaguerra [1], M. Rocca [2], E. Pagani [2], M. Radaelli [3], S. Mesaros [3], V. Martinelli [3], A. Falini [2], J. Ivanovic [4], M. Filippi [5]

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Background and aims: In neuromyelitis optica spectrum disorders (NMOSD), autoantibodies target astrocytes' aquaporin-4 (AQP4) water channel (the main regulator of CNS water homeostasis), possibly leading to increased blood-brain barrier permeability. In this work, we aim to provide an indirect estimation of brain water content in NMOSD by measuring T2-relaxation time (T2rt) and to assess whether it differs in patients having a short-term relapse.

Methods: In this multicenter MR study, T2rt was calculated from brain dual echo turbo spin echo images assuming a mono exponential decay. T2rt maps of normal appearing white matter (NAWM), gray matter (GM) and basal ganglia were obtained from 77 AQP4-positive NMOSD and 84 HC. Short-term relapses were defined as occurring within one month before or after MRI scan. Differences between NMOSD and HC were assessed with age-, sex- and site-adjusted linear models. ROC analyses were run to identify discriminators between stable and short-term relapsing patients.

Results: Compared to HC, T2rt was increased in the GM (103 vs 97ms), NAWM (88 vs 84ms) and putamen (75 vs 72 ms) of NMOSD patients ($p<0.001$ for all). Short-term relapses occurred in 20/77 (26%) of patients. T2rt cut-offs of 87 ms (NAWM and thalamus) and 88ms (caudatum) were able to discriminate between short-term relapsing and stable patients with good accuracy (AUC=0.70, 0.76 and 0.79 respectively, $p=0.027$).

Conclusion: NMOSD patients had increased T2rt values, suggesting a subclinical water accumulation in this disorder. The burden of T2rt alterations might be useful for identifying patients with incipient or recent relapses.

Disclosure: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

OPR-160

Long term safety outcomes with inebilizumab treatment in neuromyelitis optica spectrum disorder: the N-MOmentum trial

B. Cree [1], J. Bennett [2], B. Weinshenker [2], D. Wingerchuk [3], F. Paul [4], H. Kim [5], S. Pittock [2], K. Fujihara [6], G. Cutter [2], R. Marignier [7], O. Aktas [8], H. Hartung [8], A. Green [1], J. Drappa [2], D. She [2], D. Cimbora [2], W. Rees [2], J. Ratchford [2], E. Katz [9]

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Background and aims: N-MOmentum was a 28-week randomized trial comparing inebilizumab and placebo for neuromyelitis optica spectrum disorder (NMOSD). Treatment safety profile was comparable between groups. Participants could enter the open-label period (OLP; minimum two years), assessing long-term efficacy and safety of inebilizumab.

Methods: OLP participants received intravenous inebilizumab 300 mg every 28 weeks. A limited interim analysis was performed (full end-of-study OLP analysis due Q4 2020). Safety endpoints include treatment-emergent adverse events (AEs), severe and opportunistic infections, infusion-related reactions (IRRs), anti-drug-antibodies, immunoglobulin levels, leucocyte counts, and B-cell counts.

Results: Interim analyses showed 51/56 (91.1%) of those randomized to placebo (RP) and 165/174 (94.8%) randomized to inebilizumab (RI) entered the OLP. Mean (SD) OLP inebilizumab exposure in RP and RI groups was 2.4 (1.1) and 2.3 (1.1) years, respectively. AE incidence rates per 100 person-years were 304.5 (RP) and 251.4 (RI); most commonly urinary tract infection (UTI: 14.9; 7.2), nasopharyngitis (7.1; 6.9) and upper respiratory tract infection (4.7; 5.7), respectively. The most common serious AEs were UTI (4.7; 0.5) and pneumonia (0.8; 0.7), respectively. IRRs occurred in six (11.8%) RP- and 9 (5.5%) RI-participants. No correlations were found between infection rates and low concentrations of IgG or IgM ($p>0.05$). Two OLP participants died: one from complications of a severe NMOSD attack and one from a CNS event of unclear etiology. The full safety profile of longer-term inebilizumab treatment will be presented.

Conclusion: Interim analyses of the OLP indicate no additional safety concerns arising with multiple doses of inebilizumab in participants with NMOSD.

Disclosure: N-MOmentum was funded by Viela Bio. JLB, BGW, HJK, SJP, KF, GC, RM, OA, HPH, AJG report personal fees from Viela Bio and others. JD, DS, DC, WR, JNR, EK are employees of Viela Bio. BACC, DW, FP, report personal fees from other sources.

OPR-161

Long term efficacy outcomes with inebilizumab treatment in neuromyelitis optica spectrum disorder: the N-MOmentum trial

B. Cree [1], J. Bennett [2], B. Weinshenker [2], D. Wingerchuk [3], F. Paul [4], H. Kim [5], S. Pittock [2], K. Fujihara [6], G. Cutter [2], R. Marignier [7], O. Aktas [8], H. Hartung [8], A. Green [1], J. Drappa [2], D. She [2], D. Cimbora [2], W. Rees [2], J. Ratchford [2], E. Katz [9]

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Background and aims: The N-MOmentum study was a 28-week randomized trial comparing inebilizumab and placebo for neuromyelitis optica spectrum disorder (NMOSD). The trial met the primary endpoint of reduction in attack risk and showed benefit in the secondary endpoint of disability worsening. After the randomized controlled period (RCP), participants could opt-in to the open-label period (OLP; minimum two years) where the long-term efficacy and safety of inebilizumab was assessed.

Methods: OLP participants received inebilizumab 300 mg every 28 weeks. A limited interim analysis was performed (full end-of-study OLP analysis due Q4 2020). Efficacy endpoints included analyses of attack rates, disability-related outcomes and cumulative MRI lesion activity. Safety data is covered in a companion abstract.

Results: Interim analyses showed that 216/230 participants initially randomized and dosed opted to enter the OLP, 51/56 (91.1%) of those originally randomized to placebo (RP) and 165/174 (94.8%) of those originally randomized to inebilizumab (RI). During the RCP, 87.7% receiving inebilizumab and 60.7% receiving placebo remained attack-free. In the OLP, 87.7% in the RI group and 83.4% in the RP group remained attack-free for up to four years. At OLP baseline, mean (SD) EDSS scores were lower in the RI than the RP group; 3.82 (1.76) versus 4.16 (1.71). By OLP week 78, EDSS scores were lower than baseline in both groups; RI: 0.24 (0.87); RP: 0.12 (0.73). The full OLP efficacy profile of inebilizumab treatment will be presented.

Conclusion: Interim analyses indicate that benefits of inebilizumab seen in the RCP of N-MOmentum are maintained in the OLP.

Disclosure: N-MOmentum was funded by Viela Bio. JLB, BGW, HJK, SJP, KF, GC, RM, OA, HPH, AJG report personal fees from Viela Bio and others. JD, DS, DC, WR, JNR, EK are employees of Viela Bio. BACC, DW, FP, report personal fees from other sources.

OPR-162

Immunoglobulin kinetics and infection risk after long-term inebilizumab treatment for NMOSD

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Background and aims: Long-term use of B-cell depleting monoclonal antibodies is associated with reduced immunoglobulin (Ig) levels, increasing infection risk. The association between Ig levels and infection was assessed in the 28-week randomized controlled phase (RCP) and optional open-label period (OLP; minimum two years) of the N-MOmentum trial of inebilizumab for neuromyelitis optica spectrum disorder.

Methods: Ig levels were centrally recorded. Adverse events, including infections, were monitored. Opportunistic infections were predefined based on medical review.

Results: Ig levels were analyzed for 174/230 participants receiving inebilizumab for 4.75 years. There was a 35% mean decrease in total Ig with inebilizumab. Mean percent change from baseline was -62% for IgM, -50% for IgA and -30% for IgG. During the RCP, the rate of infection per 100 person-years was 140.2 (placebo) and 138.1 (inebilizumab). Infection rates per 100 person-years were lower in the OLP than the RCP: year 2: 69.9, year 3: 61.5, and year 4: 62.3 (follow-up: 614.6 person-years). The most common infections were nasopharyngitis, upper respiratory tract infection, urinary tract infection, bronchitis and influenza. The proportion of participants with an infection was similar for those with IgG levels below and above lower limit of normal (78.9% vs. 72.9%). Eight participants had IgG level <300 mg/dL at least once. The proportion of participants with infection did not differ between those with IgG<300 mg/dL and IgG 700 mg/dL (75.0% vs. 72.9%).

Conclusion: Despite declining Ig levels, infection rate did not increase with long-term inebilizumab treatment or differ between participants with normal and low IgG.

Disclosure: N-MOmentum was funded by Viela Bio. B. Greenberg has received consulting fees from various sources, including Viela Bio. D. She and E. Katz are employees of Viela Bio. B.A.C. Cree reports personal fees for consulting from other sources.

OPR-163

Satralizumab in adults with AQP4-IgG seropositive NMOSD: Efficacy and safety results from the phase 3 SAkura studies

J. Bennett [1], E. Fox [2], B. Greenberg [3], B. Weinshenker [4], K. Blondeau [5], K. Weber [5], S. Gholizadeh [6], D. Stokmaier [5], H.-C. Von Büdingen [5], A. Traboulsee [7]

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Background and aims: Satralizumab reduced the risk of protocol-defined relapse (PDR) in two randomized, phase 3 clinical trials in neuromyelitis optica spectrum disorder (NMOSD): SAkuraSky (satralizumab in combination with baseline immunosuppressants; NCT02028884), and SAkuraStar (satralizumab monotherapy; NCT02073279). We assessed the efficacy and safety of satralizumab in adults with AQP4-IgG-seropositive (AQP4-IgG+) NMOSD.

Methods: Patients received satralizumab 120mg or placebo at Weeks 0, 2, 4, and Q4W thereafter. Using data from the double-blind period, between-group comparisons were made for time to first PDR, and the rates of adverse events (AEs), serious AEs, infections, and serious infections. Laboratory values were also compared. To assess longer-term safety, data from the overall satralizumab treatment (OST) periods were evaluated (all patients receiving one dose of satralizumab in the double-blind and/or open-label extension periods; cut-off: 7 June 2019).

Results: 116 AQP4-IgG+ adults were included. Satralizumab significantly reduced PDR risk vs placebo in SAkuraSky (78% reduction) and SAkuraStar (74% reduction), with higher proportions of relapse-free patients at Week 96 (Figure). Rates of AEs and serious AEs were similar between treatment groups in both studies; infection and serious infection rates were not higher in the satralizumab groups vs placebo, and did not increase with additional satralizumab exposure in the OST period (Table). Decreases in neutrophil and platelet counts and elevations in liver enzymes were more frequently observed with satralizumab vs placebo; these were not associated with serious infections or bleeding events.

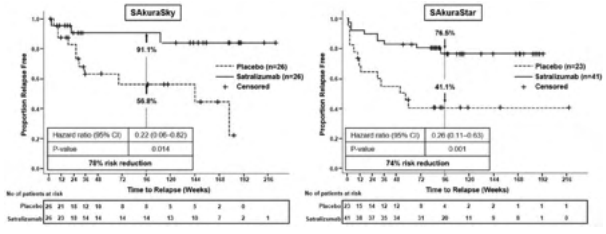

Figure – Time to first protocol-defined relapse in SAkuraSky and SAkuraStar

	SAkuraSky (combination therapy)			SAkuraStar (monotherapy)		
	Double-blind period		OST period	Double-blind period		OST period
Events per 100 PY (95% CI)	Placebo (n=26; 33.0 PY)	Satralizumab (n=26; 52.7 PY)	Satralizumab (n=44; 137.4 PY)	Placebo (n=23; 26.8 PY)	Satralizumab (n=41; 80.4 PY)	Satralizumab (n=62; 150.6 PY)
AEs	657.5 (572.9–751.0)	458.9 (402.9–520.5)	417.9 (384.4–453.5)	519.7 (436.9–613.6)	440.5 (395.8–488.9)	379.8 (349.3–412.2)
Serious AEs	30.3 (14.5–55.7)	17.1 (7.8–32.4)	16.0 (10.0–24.3)	11.2 (2.3–32.8)	17.4 (9.5–29.2)	12.6 (7.6–19.7)
Infections	184.8 (141.4–237.4)	115.7 (88.5–148.6)	129.6 (111.3–150.1)	157.0 (113.2–212.3)	93.3 (73.4–117.0)	77.0 (63.6–92.4)
Serious infections	9.1 (1.9–26.6)	3.8 (0.5–13.7)	4.4 (1.6–9.5)	3.7 (0.1–20.8)	5.0 (1.4–12.7)	3.3 (1.1–7.8)

AE, adverse event; CI, confidence interval; OST, overall satralizumab treatment; PY, patient-years

Table – Adverse event rates in the double-blind and OST periods of the SAkura studies

Conclusion: In AQP4-IgG+ adults with NMOSD, satralizumab significantly reduced relapse risk vs placebo, was well tolerated and showed a favourable safety profile.

Disclosure: Funded by F. Hoffmann-La Roche. Writing and editorial assistance was provided by David Mayes, MChem, of ApotheCom, London, UK; ClinicalTrials.gov, NCT02028884/NCT02073279.

OPR-164

Satralizumab in patients with neuromyelitis optica spectrum disorder (NMOSD) and concomitant autoimmune disease

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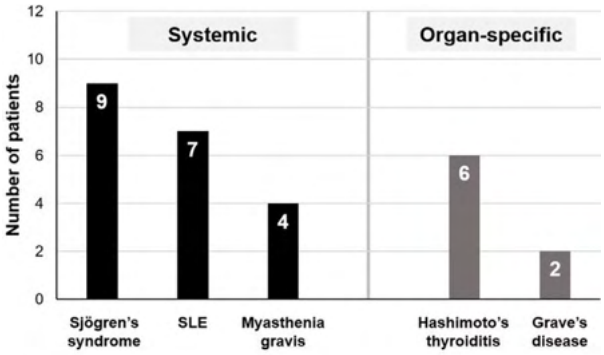
Background and aims: NMOSD is frequently associated with one or more concomitant autoimmune diseases (CAIDs). The SAkura studies (SAkuraSky [NCT02028884], SAkuraStar [NCT02073279]) enrolled diverse NMOSD populations reflective of real-world practice, including patients with CAIDs. In SAkuraSky (satralizumab in combination with baseline immunosuppressants) and SAkuraStar (satralizumab monotherapy), satralizumab reduced patients' risk of protocol-defined relapse (PDR) versus placebo and had a favourable safety profile. We evaluated the efficacy and safety of satralizumab in NMOSD patients with CAIDs from the SAkura studies.

Methods: This analysis used pooled data from patients with a medical history of CAIDs in the intention-to-treat population of the SAkura studies. The incidence of PDRs in each treatment arm was reported. Safety was evaluated throughout the double-blind period using adverse event (AE) rates per 100 patient-years.

Results: 31 patients with CAIDs were enrolled (SAkuraSky, n=15; SAkuraStar, n=16); of these, 15 received satralizumab and 16 received placebo. The most commonly reported systemic and organ-specific CAIDs are shown in the Figure. Consistent with the primary efficacy analysis, fewer patients experienced a PDR with satralizumab versus placebo (3 [20%] vs 7 [44%]). The rates of AEs, infections, and serious infections were comparable between satralizumab and placebo (Table). There was a numerically higher rate of serious AEs in the satralizumab group vs placebo, driven mainly by multiple events in one patient in SAkuraStar that were assessed to be unrelated to study treatment.



SLE, systemic lupus erythematosus.

Figure – Most common systemic and organ-specific CAIDs in the SAkura studies

	Placebo (N=16) (PY=21.11)			Satralizumab (N=15) (PY=29.66)		
	No. of AEs	Patients n (%)	Events per 100 PY (95% CI)	No. of AEs	Patients n (%)	Events per 100 PY (95% CI)
Adverse events	168	16 (100)	795.9 (680.1–925.7)	210	15 (100)	708.0 (615.5–810.5)
Serious AEs	7	5 (31)	33.2 (13.3–68.3)	13	7 (47)	43.8 (23.3–75.0)
Infections	49	10 (63)	232.1 (171.7–306.9)	52	12 (80)	175.3 (130.9–229.9)
UTI	5	3 (19)	23.7 (7.7–55.3)	13	4 (27)	43.8 (23.3–75.0)
URTI	10	3 (19)	47.4 (22.7–87.1)	5	3 (20)	16.9 (5.5–39.3)
Serious infections	1	1 (6)	4.7 (0.1–26.4)	3	3 (20)	10.1 (2.1–29.6)

AE, adverse event; PY, patient-years; URTI, upper respiratory tract infection; UTI, urinary tract infection.

Table – Adverse events in the SAkura CAIDs population

Conclusion: Satralizumab was well tolerated in NMOSD patients with CAIDs, with comparable safety and efficacy to the overall SAkura study populations.

Disclosure: Funded by F. Hoffmann-La Roche. Writing and editorial assistance was provided by Patricia Lobo (BSc) of ApotheCom, London, UK; ClinicalTrials.gov, NCT02028884/NCT02073279.

Neuroimmunology 2

OPR-165

Detection of Neuronal Surface antibodies by commercial vs in-house cell based assay: experience of a referral centre.

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Background and aims: Commercial diagnostic kits have improved the accessibility of neuronal surface antibodies (NSab) detection in suspected cases of autoimmune encephalitis. We evaluated the sensitivity of a commercial kit based on antigen-transfected-cells (cell-based assay: CBA) for the detection of NSab in samples with positive reactivity on rat-brain-immunohistochemistry (tissue-based assay: TBA).

Methods: Between 10/2016 and 10/2020, 6213 serum/CSF samples were screened using TBA. Samples showing positive reactivity were tested with commercial and in-house CBAs for NMDAR, AMPAR, LGI1, Caspr2, GABAbR and DPPX antigens, and CBAs for less common antigens (only detectable by in-house CBA).

Results: TBA showed positive reactivity in 404/6213 (6.5%) samples. Of these, 241 (60%) were negative and 163 (40%) positive by commercial CBA, confirming the presence of NSab (68 NMDAR+, 52 LGI1+, 16 AMPAR+, 11 GABAbR+, 15 Caspr2+ and one DPPX+). Of the 241 negative samples, 21 (8.7%) were positive by in-house CBA (1 NMDAR+, 11 LGI1+, two AMPAR+ and seven GABAbR+), giving false-negative results on the kit. Other 21/241 (8.7%) samples were positive for antibodies not included in the kit (13 IgLON5+, 3 SEZ6L2+, 2 mGluR1+, 1 mGluR2+, 1 mGluR5+ and 1 GABAaR+).

Conclusion: In our study the commercial CBA was not able to detect 42 (20.5%) of the 205 samples with NSab. Half of these cases were detected by in-house CBAs but not with the commercial CBA that included similar antigen specificities. In patients with high suspicion of autoimmune encephalitis and negative results on the kit we recommend to study NSab using TBA and in-house CBAs.

Disclosure: No financial disclosures

OPR-166

Pediatric neuromyelitis optica spectrum disorders in Portugal

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Background and aims: Neuromyelitis optica spectrum disorders (NMOSD) are more frequent in adulthood, with few cases reported in pediatric age. Other manifestations are known in addition to optic neuritis (ON) and transverse myelitis (TM), broadening its clinical spectrum.

Methods: Analysis and description of patients with NMOSD in pediatric age, identified in a national multicentric NMOSD Portuguese registry.

Results: From 180 NMOSD Portuguese patients identified in the national database, 20 (11,1%) were diagnosed in pediatric age, 8M: 12F. The average age of onset was 11.3 years. The initial clinical manifestation was a TM in 10 patients, four of these had ON concomitantly and two patients had a brainstem syndrome (BSS). Nine patients (45%) had pleocytosis in the CSF, with a mean cell count of 36/uL. Six exhibited anti-AQP4 antibodies, 13 anti-MOG antibodies, and one was seronegative. Four anti-AQP4+ patients had more than one relapse (three patients-2 and 1–3). Seven anti-MOG+ patients have been monophasic to date, five patients had two relapses and one had 3. The seronegative patient had three relapses. Cerebral and spinal MRI showed: ON-10, TM-9, longitudinally extensive TM (LETM)-2, brainstem lesions-2 and medullary-spinal involvement-1. In the acute phase, all were treated with IV methylprednisolone, nine with IVIg and four with plasma exchange. One died, being also diagnosed with systemic lupus erythematosus systemic and autoimmune hepatitis. Ten patients (5 anti-AQP4+/5 anti-MOG+) are on immunosuppressive therapy.

Conclusion: NMOSD may present in pediatric age. It is essential to establish the diagnosis and promptly start therapy, in order to improve the prognosis.

Disclosure: Pediatric NMOSD Portugal

OPR-167

Autoimmune Encephalitis Related to Cancer Treatment with Immune Checkpoint Inhibitors: Systematic Review

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Background and aims: Immune checkpoint inhibitors (ICPI) have revolutionized the treatment of oncological patients, but autoimmune neurological adverse events are increasingly recognized. We conducted a systematic review to determine the clinical and laboratory features of ICPI-associated autoimmune encephalitis (ICPI-AIE), to determine if this is a singular clinical entity such as limbic encephalitis or a heterogeneous condition involving extra-limbic areas and if neuronal surface or intracellular AIE antibodies are present.

Methods: We searched PubMed, The Cochrane Library and Embase for ICPI-AIE cases from the first description in 2015 until 01/2020 using standard bibliographic measures including PRISMA guidelines and pre-registration with PROSPERO (CRD42019139838).

Results: 39 studies met inclusion criteria, resulting in 54 ICPI-AIE patients (mean age 58.6 years; 43% females). Common cancers included melanoma (30%) and non-small cell lung cancer (30%). Brain metastases were found in 16 patients (30%). Most frequent ICPI was nivolumab (61%). Onset of ICPI-AIE occurred after a median of 3.5 treatment cycles, but early and late presentations were common. Non-limbic AIE was twice as frequent as limbic AIE ($p<0.05$). The most common laboratory abnormalities included bitemporal FLAIR lesions on MRI, continuous slow waves and diffuse slowing on EEG, and monocytic pleocytosis on cerebrospinal fluid analysis. Intraneuronal antibodies were more frequent than neuronal surface antibodies, and a significant predictor for lack of improvement after 1st line immunotherapy ($p<0.05$).

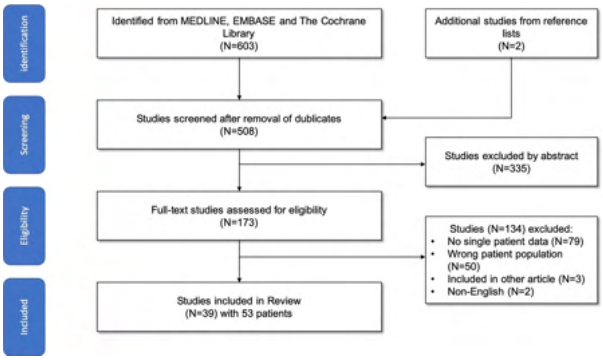

FIGURE 1 – Flow-chart of literature search

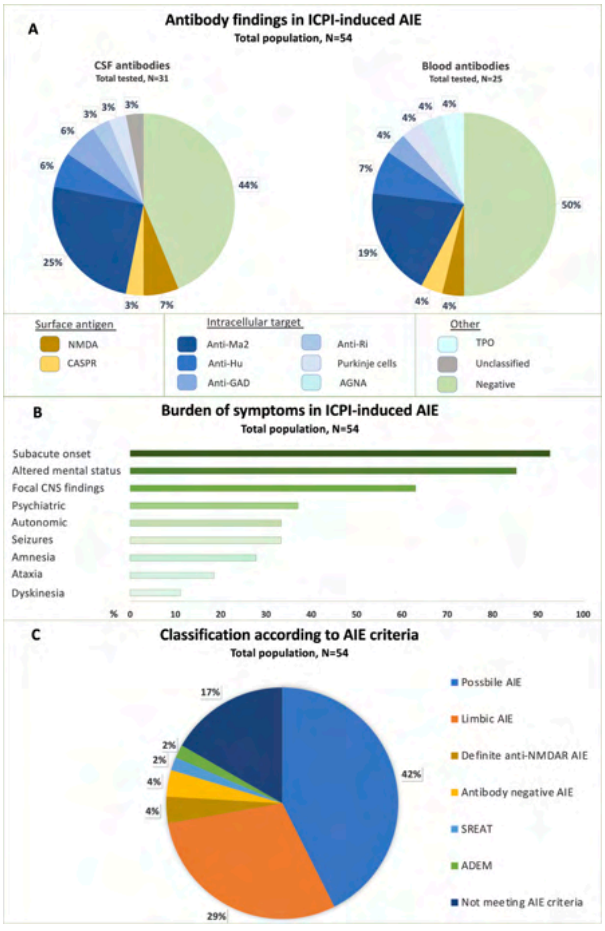

FIGURE 2 – Symptoms, antibody findings and AIE classification in ICPI-induced AIE

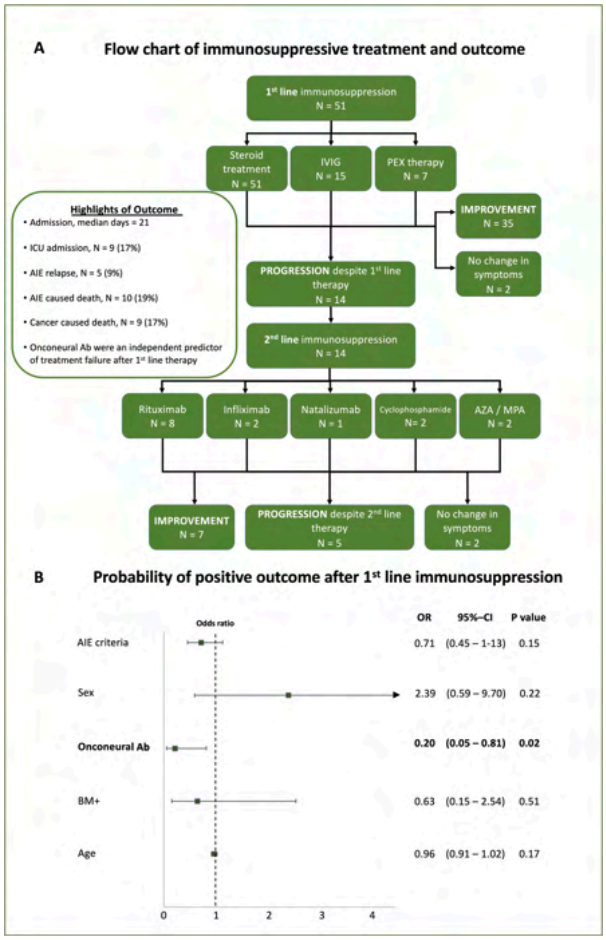

FIGURE 3 – Treatment outcome in ICPI-induced AIE

Conclusion: ICPI-AIE consists of a heterogenous group of conditions. Neurologists will likely encounter ICPI-AIE more often in the future, but important unresolved questions include the exact pathophysiological mechanisms, the epidemiology and the best treatment approaches for ICPI-AIE.

Disclosure: The authors declare that they have no conflicts of interest.

OPR-168

Involvement of the Visual Pathway in Antibody-mediated Central Nervous System Autoimmunity

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Background and aims: In autoimmune demyelinating disorders of the central nervous system (CNS), the visual system is a prominent target and retinal degeneration might serve as a generalizable biomarker of neuronal loss. However, data comparing different autoimmune demyelinating CNS disorders in patients and murine models are inconclusive. Here, we compare manifestations associated with antibodies against myelin oligodendrocyte glycoprotein (MOG-IgG), aquaporin 4 (AQP4-IgG) or unspecific isotype antibodies (Iso-IgG) in murine experimental models of CNS demyelination.

Methods: We induced active MOG35-55 experimental autoimmune encephalomyelitis (EAE) and administered AQP4-, MOG- or Iso-IgG. Visual outcome was assessed longitudinally via optomotor reflex and optical coherence tomography (OCT). Histological correlates of disease manifestations in spinal cord, optic nerve and retina were quantified using LFB/PAS staining, immunohistochemistry and -fluorescence.

Results: Disease severity was highest after application of MOG-IgG compared to AQP4-IgG or Iso-IgG. Both, MOG-IgG and AQP4-IgG administration increased disease incidence compared to Iso-IgG. Visual acuity declined in both antibody-exacerbated models over time. Histological correlates of demyelination and immune cell infiltration in spinal cord and optic nerve were found in all groups. Retinal ganglion cell numbers were decreased in chronic MOG-IgG-exacerbated EAE compared to acute phase. OCT and histological evaluation of retina and optic nerve are ongoing.

Conclusion: Previous findings that administration of MOG-IgG worsens the disease course of EAE were confirmed and corroborated by histopathological findings in the spinal cord. Although administration of AQP4-IgG did not aggravate disease symptoms compared to Iso-IgG, incidence was increased suggesting different pathophysiological mechanisms. Differences regarding the manifestations in the visual system are currently further investigated.

Disclosure: This project is supported by a research grant from the Multiple Sclerosis Society Switzerland (to AS). Besides the project funding, the authors do not declare conflicts of interest with regards to this project.

OPR-169

High incidence of NMDAR encephalitis among Austronesians: a population-based study in Sabah, Malaysia

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Background and aims: There are observations that NMDAR encephalitis may be more common among non-Caucasians. While there were several studies on the incidence of NMDAR encephalitis in children, data was scarce in adults or in full population. To our best knowledge, no study has yet been reported from South-East Asia.
Methods: A population-based study was conducted to estimate the incidence of NMDAR encephalitis in the state of Sabah, Malaysia, where the population consists predominantly of Austronesians (84%), with a Chinese minority. Registries of NMDAR encephalitis at adult and paediatric neurology referral centres, and laboratory database were searched, and medical records were reviewed for case ascertainment.
Results: From January 2015-December 2019, there was a total of 31 incident cases (29 Austronesians and two Chinese). The female-to-male ratio was 2.1:1, and 18 patients (58%) had onset 19 years. The annual incidence rate was 2.29/million (Austronesians: 2.56/million, Chinese: 1.31/million). Among paediatric population, the incidence was 3.63/million among Austronesians, and 2.59/million among Chinese.
Conclusion: Our study demonstrated higher incidence of NMDAR encephalitis among Austronesians than the predominantly Caucasian populations in Europe and USA, both in paediatric and adult populations. Racial and genetic factors, and probably environmental factors, may contribute to risks of developing NMDAR encephalitis.
Disclosure: Nothing to disclose.

OPR-170

Acute parkinsonism and small vessel cerebral vasculitis secondary to anti PD-1 therapy

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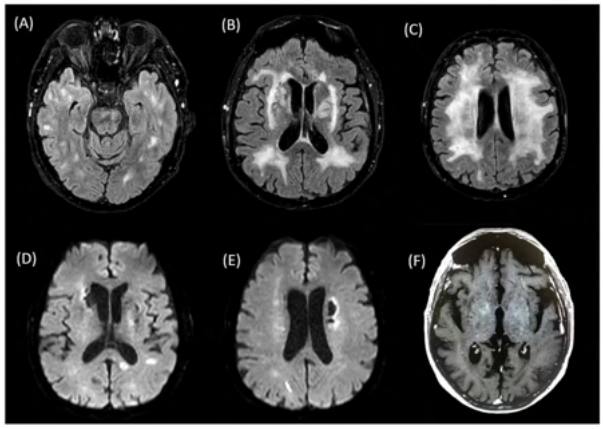
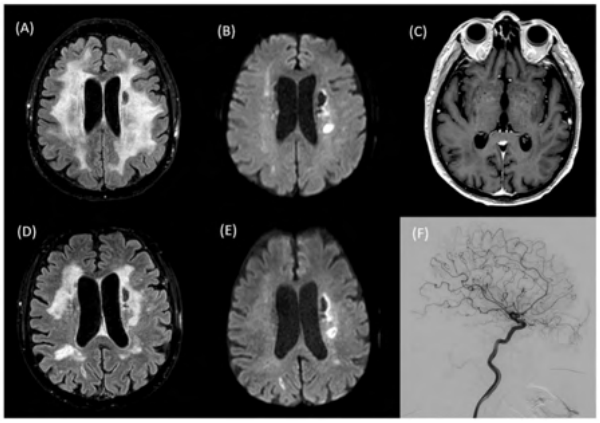
Background and aims: We describe a case of acute and reversible parkinsonism with gait apraxia related to therapy with nivolumab.
Methods: 70-year-old man, diagnosed of renal cell carcinoma with pulmonary metastases in treatment with nivolumab, who presented gait impairment, right hemiparesis and bilateral bradykinesia. Magnetic resonance imaging (MRI) revealed bilateral T2 hyperintensities, some showing restricted diffusion and others having enhancement of gadolinium, suggestive of vasculitis (Image 1). Cerebrospinal fluid analysis was negative for cytology, viral, and paraneoplastic antibody assay, with characteristics suggestive of encephalitis. Angiography showed no abnormalities suggestive of large or medium vessel vasculitis. An immune-mediated etiology was assumed due to the use of nivolumab, and megadose of methylprednisolone was started followed by tapering, with gradual improvement of motor function, parkinsonism, and gait apraxia. A second brain MRI showed resolution of lesions that previously showed gadolinium enhancement, followed by a third MRI three months later with marked resolution of the hyperintense areas (Image 2).



Brain MRI that showed bilateral confluent fronto-parieto-temporal hyperintensities (A,B,C), with restricted diffusion at the left margin of corpus callosum and parietal lobes (D,E), and contrast enhancement of the basal ganglia and both temporal areas (F)



Second brain MRI (A,B,C) showed persistence of the confluent subcortical hyperintensities and resolution of gadolinium enhanced lesions. Third MRI (D,E) showed marked resolution of the hypersignal areas. Artheriography (F) with no signs of vasculitis

Results: Nivolumab is an immune checkpoint inhibitors (ICI) that target programmed death receptor-1 (PD-1), used in the management of some advanced cancers. Neurological autoimmunity is estimated to occur in 4.2% of patients receiving ICI monotherapy. To our knowledge, this is the first case described of autoimmune and reversible parkinsonism due to vasculitis of small cerebral vessels secondary to anti PD-1 treatment.

Conclusion: We describe a not previously reported antibody/syndrome association related to anti PD-1 therapies, which broadens the clinical spectrum of autoimmune neurologic disorders related to ICI therapies.

Disclosure: No disclosures

Motor Neurone Disease 2

OPR-171

Investigating cytoskeletal integrity in the sensory nerve fibers in healthy individuals

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Background and aims: Neurons with long neurites seem to be especially vulnerable in motor neurone diseases, such as amyotrophic lateral sclerosis (ALS). Neurofilament light chain (NfL), a component of the neuronal cytoskeleton, is an established biomarker for ALS (Bacioglu et al. 2016). In this study we analyse the axonal diameter and the expression levels of microtubules, neurofilaments, and actin in skin biopsies of healthy individuals.
Methods: Skin biopsies of 27 men (mean age 54.2±18.9 a, from 24 a to 79 a) were immunostained for non-phosphorylated neurofilament heavy chain (npNfH), betaIII-tubulin, and actin (phalloidin). Confocal images of the dermis were analysed for the mean grey values and diameter. This study was approved by the local ethics committee. Participants gave informed written consent.
Results: Cytoskeletal components (npNfH, betaIII-tubulin, actin) drastically increased with age. NpNfH increased 2.7-fold, whereas betaIII-tubulin levels increased 3.2-fold from 24- to 75-year-old individuals. Actin showed a change of 3.8-fold from the youngest to the 62-year-old controls (peak, maximum values). Sensory axon caliber increased 2.2-fold from the 29- (1.35µm) to the 78/79-year old (2.97µm) controls. Statistical analysi (Mann-Whitney U test) showed highly significant results between each staining/caliber and age ($p<0.001$).
Conclusion: Our results suggest an age-driven 'ossification' of the axonal cytoskeleton in peripheral sensory axons, which might influence cytoskeletal functionality. These findings are in accordance with the increased susceptibility of aged individuals to motor neurone diseases. The results reported here will be validated in a second independent cohort (27 men, age 26 to 74).
Disclosure: The authors have no relevant conflicts of interest to disclose.

OPR-172

PULSE: a French multi-centric, multi-modal cohort to predict the disease progression of ALS and to define endophenotypes

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Background and aims: Amyotrophic Lateral Sclerosis (ALS), devastating disease for which no treatment can effectively slow its progression, is a complex heterogenous and multifactorial disorder influenced both by genetic and environmental factors. The development of successful neuroprotective drugs requires patients' stratification according the prognosis (for statistical power) and the drug targeted mechanism (drug efficacy) with the monitoring of biomarkers (endophenotypes).
Methods: 16 French expert ALS centers have implemented a web-based solution to prospectively collect multimodal data every three months from diagnosis up to 36 months with an objective of 1000 patients. Data include clinic, ALSFRS, muscular testing, cognitive assessment, electrophysiology (EMG, MUNIX, triple stimulation), respiratory assessment, polysomnography, biological samples and 3T MRI.
Results: PULSE cohort includes 430 ALS patients and 70 healthy controls. All data are collected into an eCRF. A central biobank ensures quality and conformity of all biological samples (DNA, plasma, serum, CSF, biopsies). A. central brain- and spinal cord-imaging bank ensure the quality of all MRIs sequences. Statistical approaches with joint latent class analyses, linear mix model analysis and machine learning will be used.
Conclusion: PULSE is the largest prospective multi-centric French cohort of ALS patients followed from the diagnosis. It will allow 1) to define the prognosis factors of the survival, 2) to define prognosis factors of the rate of ALSFRS decline, 3) to determine endophenotypes according to prognosis factors and physiopathological biomarkers in order to develop relevant clinical trials. PULSE is funded by the French Charity association ARSLA
Disclosure: No conflict of interest

OPR-173

Chinese-German comparison of mutational and clinical features of ALS patients with SOD1 mutations

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Background and aims: The antisense oligonucleotides therapy for ALS patients carrying SOD1 mutations is coming in soon. The genetic-phenotypic analysis of ALS patients of different ethnics will facilitate to assess potential treatment effects.

Methods: Demographic and clinical features were collected from two longitudinal cohorts in both countries. Chinese and German patients carrying SOD1 mutations were compared with regard to mutational distribution, age of onset, site of onset, BMI at diagnosis, diagnostic delay, progression rate, and survival.

Results: A total of 66 Chinese and 84 German patients with 69 distinct SOD1 mutations were identified (Figure1). The most common mutation in both populations was p. His47Arg. It was found in eight Chinese and two German patients and consistently showed a benign course of disease in both countries. Across all mutations, Chinese patients showed a younger age of onset (43.9 vs 49.9 years, p=0.002), a higher proportion of young-onset cases (62.5% vs 30.7%, p<0.001) and a lower BMI at diagnosis (22.8 vs 26.0, p<0.001) compared to German patients (Table1). Although riluzole intake was less frequent in Chinese patients (28.3% vs 81.3%, p<0.001), no difference in survival was observed. Female patients had a longer survival compared to male patients (Figure2).

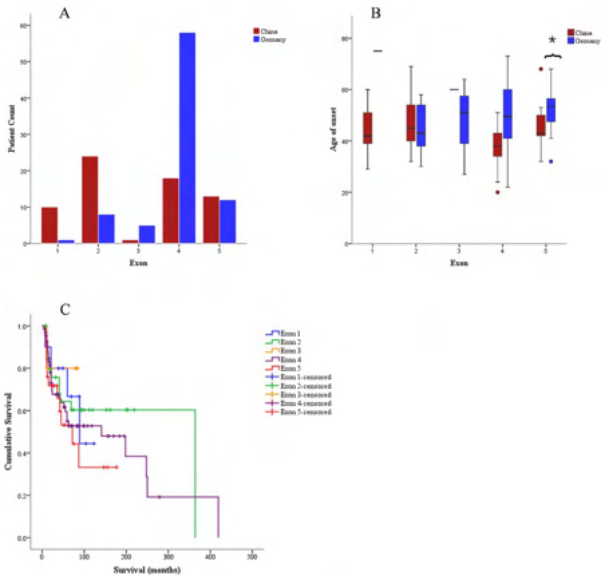

Figure 1. Demographic and clinical features of patients carrying SOD1 mutations by exons.

Table 1 Clinical characteristics of *SOD1* mutation populations

	Total (data available)	China	Germany	P value**	Male	Female	P value**
Nominal variables, n (%)							
Numbers of subjects	150	66	84		80	64	
Sex, male	80 (54.4%) [144]	39 (59.0%)	41 (57.0%)	0.70	-	-	-
Familial ALS	114 (79.6%) [143]	47 (71.2%)	67 (84.8%)	0.05	64 (83.1%)	44 (71.0%)	0.09
Juvenile ALS (< 25 years)	3 (2.2%) [139]	2 (3.1%)	1 (1.3%)	-	-	2 (3.8%)	-
Young onset ALS (25–45 years)	63 (47.3%) [139]	40 (62.5%)	23 (30.7%)	<0.001	30 (39.5%)	33 (61.4%)	0.10
Site of onset, spinal	114 (94.3%) [121]	57 (91.9%)	57 (96.7%)	0.21	66 (94.3%)	48 (94.1%)	0.99
Pure LMN	16 (10.0%) [160]	9 (17.3%)	7 (10.0%)	0.41	8 (10.0%)	8 (10.0%)	1.00
riluzole	84(53.0%) [161]	18 (28.0%)	59 (81.3%)	<0.001	32 (40.4%)	22 (41.0%)	0.14
Continuous variables, mean (95%CI)							
Age of onset (years)	47.2 [44.2–49.1] [139]	43.9 [41.6–46.2]	49.9 [47.8–52.0]	0.002	48.7 [46.0–51.4]	45.3 [42.6–48.1]	0.08
BMI at diagnosis	24.1 [23.2–24.9] [91]	22.8 [21.9–23.7]	26.0 [24.7–27.4]	<0.001	24.4 [23.3–25.4]	23.8 [22.4–25.2]	0.49
Continuous variables, median (IQR)							
Diagnostic delay (months)	12.0 [6.0–35.0] [107]	14.5 [6.0–36.0]	11.0 [6.0–32.0]	0.19	11.0 [5.0–24.0]	15.0 [5.0–47.0]	0.01
ALS FRSR at diagnosis	41.0 [36.0–45.0] [134]	42.0 [38.0–46.0]	40.0 [35.0–44.0]	0.04	41.0 [36.0–46.0]	40.0 [34.0–44.0]	0.50
Early progression rate (onset to first visit)	0.42 [0.14–0.90] [134]	0.33 [0.10–0.90]	0.46 [0.13–0.91]	0.79	0.49 [0.20–0.82]	0.31 [0.13–1.00]	0.48
Late progression rate (first to last visit)	0.26 [0.09–0.79] [69]	0.28 [0.08–0.80]	0.17 [0.11–0.77]	0.89	0.30 [0.11–0.90]	0.20 [0.09–0.63]	0.32
Survival (months)	141.0 [21.0–364.0] [140]	NA	198.0 [22.0–364.0]	0.90	60.0 [17.0–250.0]	240.0 [44.0–419.0]	0.001
Follow-up period*	24.0 [7.0–48.0] [160]	30.0 [18.0–42.0]	15.0 [3.0–41.0]	0.06	15.0 [7.0–31.0]	30.0 [9.0–48.0]	0.12

** χ^2 test for nominal variables; *t* test for normally distributed continuous variables; Mann-Whitney U test for non-normally distributed continuous variables; log-rank test for overall survival. Bold p-values are significant. LMN: lower motor neuron

Table 1.Clinical characteristics of SOD1 mutation populations

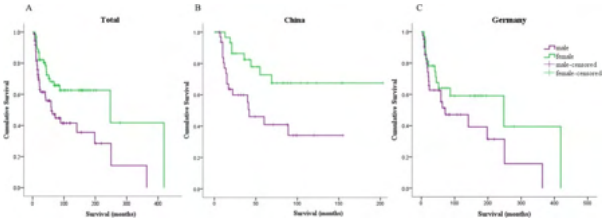

Figure 2. Sex and Survival. Kaplan Meier curves show survival for male (purple) and female (green) patients overall (A: p=0.005), in China (B: p=0.009), and Germany (C: p=0.15).

Conclusion: Our data demonstrate the distinct mutational and clinical spectrums of SOD1-mutant patients in Asian and European populations. Clinical phenotypes seem to be influenced by mutation-specific and ethnicity-specific factors simultaneously, indicating that there is no monocausal relationship between the genetic mutations and clinical phenotypes. Further large-scale transethnical studies are needed to clarify determinants and modifiers of SOD1 phenotypes.

Disclosure: All authors have nothing to disclose.

OPR-174

A systematic review of extra-motor symptom evaluation in clinical trials for amyotrophic lateral sclerosis.

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Background and aims: Amyotrophic lateral sclerosis (ALS) is increasingly recognised as a multi-system disorder. Extra-motor symptoms such as cognitive impairment, behavioural change, neuropsychiatric symptoms, sleep disturbances, fatigue, sialorrhea, and pain are common in, and impactful upon, people with ALS. We aimed to systematically review historical clinical trials in ALS to identify if extra-motor features of ALS were explored as outcome measures and if so describe the tools used.
Methods: We reviewed clinical trials of investigative medicinal products in ALS, since the licensing of riluzole. Trial registry databases were searched for Phase II, III or IV trials registered, completed or published between 01/01/1994 and 16/09/2020. No language restrictions applied. We evaluated the use of assessment tools to investigate extra-motor symptom as outcome measures.
Results: 237 clinical trials were included in this review for use of outcome measures. These trials evaluated cognitive impairment (16 trials, 6.8%), behavioural change (38, 16%), neuropsychiatric symptoms (75, 32%), sleep disturbances (12, 5%), fatigue (18), 8%, saliva (182, 77%) and pain (55, 23%). 29 trials (12%) did not include any assessment of extra-motor symptoms. 51 versions or combinations of assessment tools were utilised in these trials.
Conclusion: Extra-motor symptoms have been under-evaluated in trials for people with ALS. Where evaluated, this has been primarily using assessment tools which are not specific to ALS or the extra-motor symptom, which may affect the validity of conclusions drawn regarding the impact of candidate drugs.
Disclosure: Nothing to disclose.

OPR-175

SUNFISH Part 2: 24-month efficacy and safety of risdiplam in patients with Type 2 or non-ambulant Type 3 SMA

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Background and aims: Spinal muscular atrophy (SMA) is a severe, progressive, neuromuscular disease caused by reduced levels of the survival of motor neuron (SMN) protein due to deletions/mutations of the SMN1 gene. A second gene, SMN2, produces only low levels of functional SMN protein. Risdiplam (EVRYSDI™), a centrally and peripherally distributed, oral SMN2 pre-mRNA splicing modifier, received FDA approval for the treatment of patients with SMA, aged two months and older.
Methods: SUNFISH (NCT02908685) is a multicentre, 2-part, randomised (2:1, risdiplam:placebo),

placebocontrolled, double-blind study in patients with Type 2 or 3 SMA (inclusion criteria: 2–25 years at enrolment). Part 1 (n=51) assesses safety, tolerability, and pharmacokinetics/pharmacodynamics of different risdiplam doses. Part 2 (n=180) assesses efficacy and safety of the Part 1-selected risdiplam dose versus placebo in Type 2 and non-ambulant Type 3 SMA. Individuals were treated with risdiplam or placebo for 12 months; all individuals then received risdiplam until Month 24. At Month 24, patients were offered the opportunity to enter the open-label extension.

Results: The primary endpoint of SUNFISH Part 2 was met. A statistically greater change from baseline in the total score of the 32-item Motor Function Measure (MFM32) was observed at Month 12 in patients treated with risdiplam (N=120) compared with those who received placebo (N=60). No treatment-related safety findings leading to withdrawal were reported. Here, we present 24-month SUNFISH Part 2 data.

Conclusion: SUNFISH Part 2 is ongoing and will provide further data on the long-term efficacy and safety of risdiplam in a broad population of children, teenagers and adults.

Disclosure: This study was sponsored by F. Hoffmann-La Roche Ltd, Basel, Switzerland. Writing and editorial assistance was provided by MediTech Media UK, in accordance with GPP3 guidelines, and funded by F. Hoffmann-La Roche Ltd.

Neurogenetics 2

OPR-176

Epigenetic and Radiomics study of progestin-associated meningiomas

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Background and aims: The role of progestins in meningioma development has been described since 1980. Recent reports highlight an increased incidence of meningioma in patients treated with cyproterone acetate (CPA). Molecular analyses underlined the involvement of other tumorigenesis pathway than the NF2 mutations, the main known meningioma driver. However, the epigenetic and radiomics profile of progestin-associated meningioma (PAMs) remain unknown.
Methods: We retrospectively identified 44 patients diagnosed with a meningioma after a minimum of one year of progestin treatment from our hospital database. We established a control cohort of 20 sporadic meningioma. We extracted 150 radiomics features/MRI/ patient (Sophia Radiomics software). Statistics analyses and machine learning algorithms were performed using Rv3.6.2. We obtained global DNA methylation profiles (DFKZ classification, https://www.molecularneuropathology.org/mnp) in a subgroup of 11 operated PAMs using EPIC850K (Illumina) array.
Results: We analyzed 76 meningioma (65% of skull base, 35% of convexity) from 44 patients. Median age at diagnosis was 54 years, and mean progestin treatment duration was 18.2 years. 50% of PAMs (38/76) regressed after cessation of progestin treatment with a median regression rate of 20%/year while 33% of PAM (25/76) stabilized and 17% (13/76) pursued growth. Decrease of small diameter (p=10^-6) and texture homogeneity (p=10^-5) were the main changes in radiomics features. Methyloma study highlighted a relatively homogenous epigenetic profile corresponding to MCben2, a benign meningioma subtype.
Conclusion: Our study is the first radiomics and epigenetic analysis of PAMs. It enriches the knowledge on molecular landscape of PAMs, highlighting their molecular homogeneity and it provides extensive radiomics characterization.
Disclosure: This research was undertaken with the assistance of resources and services from the Sophia Genetics Data Science department.

OPR-177

Single nucleotide polymorphisms as possible phenotype modifiers in charcot-marie-tooth 1a disease: a cohort study

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Background and aims: There is a great variability of phenotype expression in Charcot-Marie-Tooth type 1A (CMT1A) even within the same family. To date, no univocal explanations are available. Single nucleotide polymorphisms (SNPs) could play a role in modulating phenotype in CMT1A patients but no definite evidence is available.
Methods: 23 CMT1A patients were enrolled. SNPs rs4280262 in LITAF, rs6875902 , rs3763022 and rs2304034 in SH3TC2, rs10910527, rs4649265, rs7536385 and rs1547740 in SIPA1L2, H63D and C282Y in HFE were analyzed. Each patient was assessed by several validated scales in order to quantify sensory and motor involvement.
Results: The presence of LITAF rs4280262, SH3TC2 rs3763022, SIPA1L2 rs10910527, SIPA1L2 rs4649265 and SIPA1L2 rs7536385 was associated with a more severe phenotype. SH3TC2 rs2304034, SH3TC2 rs6875902 and SIPA1L2 rs1547740 did not appear to have an effect.. HFE H63D was associated with a lower strength in foot dorsiflexion (p=0.022). Patients were classified according to the number of polymorphisms. Correlation analysis showed a positive relationship between the number of SNPs and the burden of disability in the upper (p=0.012) and lower limbs (p=0.019) and the severity of sensory involvement (p=0.025) and an inverse correlation with the meters walked at 6MWT (p=0.011).
Conclusion: SNPs could play a role in modulating CMT1A phenotype. We observed a possible role also for the H63D polymorphism in HFE which was not previously described. Our results showed a possible summation effect of SNPs in influencing the phenotypical expression of the disease. Certainly, larger case studies are needed in order to confirm these observations.
Disclosure: Nothing to disclose.

OPR-178

Genetic study of Italian families affected by small fibre neuropathy identified variants in predisposing pain phenotype

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Background and aims: Peripheral Neuropathy (PN) affects 2.4% of people and almost 50% of general population is known to have pain-related symptoms. Genetic studies in painful PN (PPN) revealed that Voltage Gated Sodium Channels (VGSCs) genes are involved in pain amplification. Here we aimed to broaden the genetic aspect of PPN by using whole exome sequencing (WES).
Methods: Six families with PPN were selected having at least one affected member, positive neurological examination and pain questionnaire result with numerical rating score ≥4. Variants were filtered with manually curated gene panel, allele frequency (AF) and computational predictors. Segregation causative/protective models were applied according to pedigree and sharing models were applied after grouping probands of each family.
Results: According to segregation causative and protective model, we found 129 and 112 variants respectively (AF≤10%) across families. Among genes shared between two families with causative approach, variants were observed in SCN9A, SV2C and DST, whereas protective variants in TRPM2 and LRP1. In shared model, we identified 21 variants and 53 genes shared across ≥3 probands. Among shared genes with predicted high-impact variants in probands were observed in SCN9A, SCN7A, P2RY4, P2RX7, TRPV4 and TRPM1.
Conclusion: WES approach appears powerful in mutation detection and in revealing new genotype-phenotype association. In addition to VGSCs, other gene families including Transient Receptor Potential and Purinergic Receptor seem to play a role in pain modulation. The same approach will be replicated on new families already sequenced before proceeding with ad hoc functional experiments to deepen the role of genes in painful phenotype.
Disclosure: FE:Novartis,Sanofi Genzyme,Almirall,Merck-Serono. FMB:Teva Pharma Industries, Sanofi Genzyme, Merck-Serono, Biogen Idec, Roche, Medday, Excemed. MF:Bayer,Biogen Idec, Merck-Serono, Novartis, Roche, Sanofi Genzyme, Takeda, Teva Pharma

OPR-179

Genotype-phenotype correlations in VCP disease: Results of an International Multicentric Study (The VCP study group)

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Background and aims: Valosin-containing protein (VCP) disease, an adult autosomal dominant disorder caused by mutations in the VCP gene leading to disabling weakness, Paget's disease of bone (PBD) and Fronto temporal dementia, is frequently misdiagnosed with other muscle or motor neuron entities.
Aim: to describe the clinical and genetic features of a large cohort of VCP mutated patients and investigate genotype – phenotype correlations.
Methods: We collected clinical and genetic data from patients with confirmed mutations in the VCP gene from 25 centres in 12 countries.
Results: 128 patients included (70% males, mean age 55.54 years old; SD 9.6). Age at symptom onset 45.42 y.o (SD 10) Diagnostic delay 7.74 years (SD 6). 98% had an heterozygous mutation. c.464G>A and c.463C>T were the most frequent variants. At beginning, 30% had proximal symmetric lower limbs (LL) weakness and 10% LL and/or upper limb (UL) asymmetric weakness. At enrolment, 89% had proximal LL weakness, 56% axial weakness, 44% respiratory symptoms, 22% PBD and 20% cognitive impairment. Dysautonomia (26%) and upper motor neuron symptoms (9%, UMN) appeared within the first two years. 58% required walking assistance at 9,14 (SD 5) y. from onset. The c.463C>T variant had an earlier onset (37.4y.o, SD 7.5) and greater UL and axial weakness. Sixteen patients died (main reason respiratory insufficiency) at a mean of 12 (SD 7) y. from onset.

Conclusion: VCP disease resembled a LGMD, however, the early presence of dysautonomia, UMN and the rapid loss of ambulation should raise awareness of VCP. The c.463C>T variant had a more severe phenotype.
Disclosure: Nothing to disclose.

OPR-199

Evidence of shared biological pathway between Parkinson's disease and psychiatric disorders.

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Background and aims: Epidemiological studies have suggested several possible associations between Parkinson's disease (PD) and psychiatric traits. By studying shared genetic architecture and biology, we can dissect common pathways and suggest new targets for drug development.
Methods: We selected genome-wide association studies (GWASs) summary statistics from recently published PD GWAS and 12 traits from Psychiatric Genomics Consortium. We have applied linkage-disequilibrium score regression (LDSC) to study the genetic correlation between the traits. Next, to identify significant associations between complex traits and gene expression in different tissues, we performed a transcriptome-wide association study (TWAS) using the FUSION software. Correlation between each pair of disorders was calculated using the RHOGE package. We performed a cross-tissue analysis of gene expression using the UTMOST package and identified genes significantly associated with both PD and psychiatric traits. At the next step, we performed gene pathway analysis to identify common pathways across traits.
Results: We found a genetic correlation between PD and attention deficit hyperactivity disorder(ADHD). Analysis of gene expression identified a significant negative correlation between PD and ADHD only in the cortex but not in the other tissues. Interestingly, we found a negative correlation between alcohol consumption and PD in the hypothalamus, hippocampus and a positive correlation between cannabis dependence and PD in the cerebellar hemisphere. In the cross-tissue analysis, we found several genes significant for PD and several psychiatric traits (ADHD, anorexia, alcohol consumption, bipolar disorder and schizophrenia).
Conclusion: In our study, we have found common genes and pathways for PD and psychiatric traits, which could explain epidemiological associations.
Disclosure: Nothing to disclose

Sleep Disorders

OPR-180

Sleep patterns of Parkinson's disease patients and their relation to neural activation during motor learning

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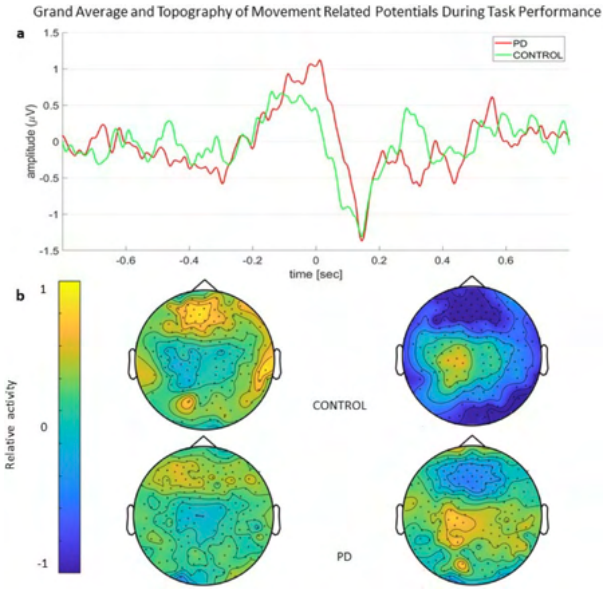
Background and aims: Sleep disorders (SD) are tightly correlated with Parkinson's disease (PD) and considered a major contributor to its pathogenesis. The motor decline associated with the disease can manifest as difficulty in the generation of a motor plan and the development of procedural learning. A possible explanation is that disease specific sleep-abnormality, saboteurs motor-learning consolidation, and prevent an efficient stabilized learning. This study is designed to elucidate the role of SD in the pathophysiology of PD, characterize sleep patterns, and examine their relationship to neuronal activity underlying motor-learning among PD patients and healthy older adults.
Methods: By employing a self-designed motor learning task and high-density EEG recording, this study examines the behavioral and neural correlates of motor-learning among PD patients and healthy controls. By combining polysomnography sleep recording, this study will further characterize the relationship between quantitative sleep patterns and cortical activity during motor-learning.
Results: Preliminary data confirm task validity and provides group behavioral results. Response-locked EEG activity during task performance supports the hypothesis for extended activation patterns among PD subjects and provides neuronal correlations of motor-learning.



a. grand averaged response-locked activation during motor task performance. Signals are averaged between five control subjects (green line), and 9 PD subjects (red line). b. control (top plots) vs. PD (bottom)

Conclusion: this study focuses on the triple bond of PD, sleep, and motor learning with the goal of providing insights into the underlying pathophysiology of neurodegeneration. Initial group differences already emerge in both behavioral and neuronal correlates of motor learning. In the future, more data collection will enable the extraction of sleep patterns characterization, sleep-dependent motor-learning and EEG patterns, and establish group differences among PD patients and age-matched control.
Disclosure: I have nothing to disclose

OPR-181

Inter-rater sleep stage scoring reliability between two sleep centres and an automated artificial-intelligence algorithm

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Background and aims: To integrate automatic sleep stage scoring algorithms based on artificial intelligence (AI) in clinical practice, their generalizability to different cohorts needs to be evaluated. In this study we evaluate inter-scorer reliability (IRR) for sleep stage scoring between two sleep centres and the previously validated AI-based Stanford-STAGES algorithm (Stephansen et al., 2018).

Methods: Full night polysomnographies of 1066 subjects (53.47% men, median age 54 years) from the population-based Study of Health in Pomerania (Germany) were included. Sleep stages were manually independently scored by experts at the Hospital Charité, Center of Sleep Medicine, Berlin (Germany) and at the Department of Neurology, Medical University of Innsbruck (Austria). Sleep stages were also automatically scored with the Stanford-STAGES algorithm. For each subject, IRR was evaluated with Cohen's kappa () by comparing 1) Innsbruck to Berlin scorings (INN-vs-BER); 2) Innsbruck to automatic scorings (INN-vs-AUTO); 3) Berlin to automatic scoring (BER-vs-AUTO); and 4) both manual to automatic scorings (MAN-vs-AUTO). Mean and standard deviation of values were calculated across participants.

Results: Overall average sleep stage scoring agreement was substantial for INN-vs-BER (=0.66±0.13), INN-vs-AUTO (=0.68±0.14) and MAN-vs-AUTO (=0.61±0.14), and moderate for BER-vs-AUTO (=0.55±0.15).

Conclusion: The agreement between manual scorers was in line with previously published findings. The overall substantial agreement between manual and automatic scorings suggests that the Stanford-STAGES algorithm is generalizable to new cohorts. Despite future independent studies are needed, we demonstrate that integration of AI methods for automated sleep stage scoring in clinical practice is a goal that could be achieved in the near future.

Disclosure: Nothing to disclose

OPR-182

REM sleep without atonia and nocturnal body position in prediagnostic Parkinson's disease

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Background and aims: Sleep disturbances and polysomnographic (PSG) alterations are features of Parkinson's disease (PD), that can already occur before PD diagnosis. The most investigated prodromal PD sleep disorder is REM sleep behavior disorder (RBD). The relation between other PSG variables and PD and its prediagnostic stages, however, is less clear.

Methods: We performed a retrospective cross-sectional case-control study in 63 PD subjects (33 subjects that underwent a PSG before PD diagnosis [13 with and 20 without RBD] and 30 subjects that underwent a PSG after PD diagnosis) and 30 control subjects. PSGs were analyzed for sleep stages, different REM sleep without atonia (RSWA) variables, body position, arousals, periodic limb movements, REM density and apnea-hypopnea index.

Results: Our results show higher amounts of all RSWA subscores in subjects with PD and prediagnostic PD (with and without RBD) (table 1). Total RSWA, tonic RSWA and chin RSWA severity were significant predictors for the prediagnostic PD group without RBD (table 2). Our study also shows a higher supine body position percentage in all (prediagnostic) PD groups, which is the highest in PD and positively correlates with time since diagnosis.

Sleep time in supine body position (%)	17.73 (26.79)	46.17 (67.30)	42.40 (49.57)	78.57 (45.04)	**<0.001**
Sleep time in nonsupine body position (%)	83.10 (26.91)	49.07 (67.2)	57.71 (49.57)	23.99 (58.14)	**<0.001**
RSWA total (%)	0.64 (3.48)	3.21 (17.31)	33.73 (41.08)	7.85 (26.52)	**<0.001**
RSWA tonic (%)	0.00 (0.00)	2.25 (6.97)	28.57 (42.92)	3.01 (16.96)	**<0.001**
RSWA phasic total (%)	0.00 (3.39)	0.24 (12.32)	16.12 (33.98)	12.41 (17.07)	**<0.001**
- Chin	0.00 (0.00)	0.00 (3.71)	11.76 (20.49)	1.22 (9.62)	**<0.001**
- leg	0.00 (3.38)	0.00 (1.04)	6.45 (21.24)	5.73 (9.80)	**<0.001**
RSWA chin (%)	0.00 (0.00)	3.22 (8.51)	31.72 (33.15)	4.43 (17.08)	**<0.001**

Table 1: Results of all RSWA subscores and body position. Medians (interquartile range) are given. PSG=polysomnography, PD= Parkinson's disease, RBD= REM sleep behavior disorder. REM=Rapid-Eye-Movement. RSWA=REM sleep without atonia, AHI=Apnea/hypopnea index. N= number. PLMS= periodic limb movements of sleep. Kruskal Wallis tests were used, P values are corrected for multiple comparison and significant p values (p<0.003) are shown in bold.

Table 1: Polysomnographic characteristics of the study population.

Predictor	Prediagnostic PD RBD −		Prediagnostic RBD +		PD	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
RSWA total	1.26 (1.06-1.50)	**0.010**	1.37 (1.15-1.64).	**0.001**	1.31 (1.10-1.56)	**0.003**
RSWA tonic	1.80 (1.14-2.82).	**0.011**	2.00 (1.27-3.14)	**0.003**	1.85 (1.18-2.90)	**0.008**
RSWA phasic total	1.19 (1.02-1.40)	0.032	1.32 (1.13-1.55)	**0.001**	1.28 (1.10-1.50)	**0.002**
- RSWA phasic leg	1.01 (0.80-1.27)	0.927	1.32 (1.10-1.59)	**0.004**	1.30 (1.08-1.56)	**0.005**
- RSWA phasic chin	2.16 (1.02-4.59)	0.045	2.45 (1.15-5.21)	0.020	2.21 (1.04-4.68)	0.039
RSWA chin total	1.66 (1.12-2.46)	**0.012**	1.83 (1.23-2.72)	**0.003**	1.70 (1.14-2.51)	**0.009**
Supine body position	30.7 (2.16-437.472)	**0.012**	40.97 (2.63-701.31)	**0.008**	570.113 (36.57-8888.23)	**<0.001**
Interaction supine body position and total RSWA	0.816 (0.49-1.36)	0.433	0.892 (0.533-1.50)	0.670	0.84 (0.50-1.39)	0.491
Interaction supine body position and chin RSWA	1.02 (0.28-3.69)	0.976	1.35 (0.37-4.92)	0.652	1.14 (0.315-4.14)	0.840

Table 2. The multinominal logistic regression analyses results are shown for each group with the control group as reference category. Odds ratios (95% confidence interval) and P values are given. PD=Parkinson's disease, RBD=REM sleep behavior disorder, RSWA is REM sleep without atonia. P values are corrected for multiple comparison and significant p values (p<0.017) are shown in bold.

Table 2: The multinominal logistic regression analyses results

Conclusion: These findings suggest that higher total, tonic and chin RSWA subscores, as well as nocturnal supine body position, are already present in prediagnostic PD, independently of iRBD status. Furthermore, they highlight the relevance of monitoring complications of supine body position (such as OSAS) in PD. Prospective longitudinal studies are necessary to investigate their potential role as biomarkers for prediagnostic PD patient selection and monitoring in neuroprotective trials.
Disclosure: Nothing to disclose.

OPR-183

Thyroid gland disorders increase the risk for restless legs syndrome in multiple sclerosis

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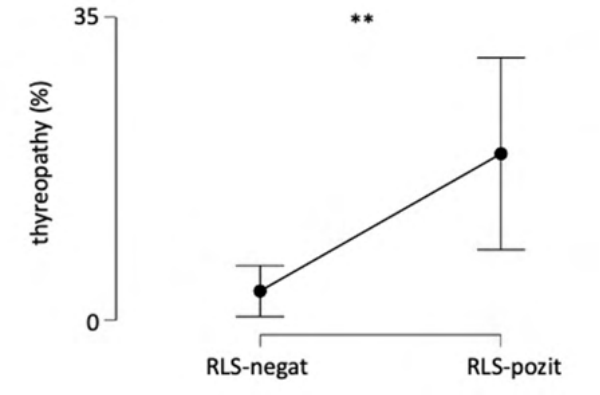
Background and aims: Multiple sclerosis (MS) is a chronic autoimmune disease of the central nervous system with various neuropsychiatric symptoms. It is known, that patients with MS are at higher risk for restless legs syndrome (RLS) what leads to increased morbidity and decreased quality of life. MS is an autoimmune disorder and patient often suffer from autoimmune thyroiditis. The purpose of our work was to find the correlation between thyroid gland disorders and RLS among patients with MS.
Methods: We collected data from 200 patients with MS from the Centre for Multiple Sclerosis at the Second Department of Neurology, University Hospital and Comenius University Bratislava. All patients were examined by trained clinician with International Restless Legs Syndrome Questionnaire and International Restless Legs Syndrome Severity Scale. We obtained additional data about age, gender, MS duration, and presence of thyroid disorder.
Results: There were significantly more patients with thyroid disorder among RLS subjects (19.2 versus 3.4%, p<0.001), the risk for RLS was 6.81-times higher in patients with thyreopathy (95% CI 2.21–21.02).



Prevalence of thyroid gland disease in RLS-negative and RLS-positive patients

Conclusion: We confirmed that MS patients with thyroid gland disorder are at higher risk for RLS. When unrecognised, it can lead to sleep disturbances, excessive daytime sleepiness and fatigue. All this increase risk of anxiety and depression, as well as the risk of cardio- and cerebrovascular disorders. That's why patients with MS must be actively screened for restless legs syndrome, especially when they suffer from any thyroid gland comorbidity.
Disclosure: Nothing to disclose.

Tuesday, June 22 2021
Epilepsy: Stroke and acute presentations

OPR-061

Epilepsies associated with anti-neuronal antibody positivity: the experience of a Portuguese tertiary centre

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Background and aims: With the advent of anti-neuronal antibody testing, autoimmunity has been increasingly recognized as the possible cause of epilepsies of previously unknown aetiology, regarded as more refractory to conventional antiepileptic medications and responsive to immunotherapy.
Methods: Using the Immunology Department database from our hospital, we identified all patients with positivity in anti-neuronal autoantibody testing profiles in serum and/or CSF requested for autoimmune encephalopathy/epilepsy/dementia from 2016 to 2020, and identified those that fulfilled diagnostic criteria for epilepsy (ILAE 2014). Their clinical information was then retrospectively reviewed.
Results: Among 207 patients with positive anti-neuronal antibodies, 33(16%) fulfilled diagnostic criteria for epilepsy: 20(61%) male, median age=54-years-old at time of anti-neuronal positivity. 22 (67%) had intracelullar and 11(33%) had cell-surface antibodies. Antibodies identified included anti-GAD65(n=8;24%), anti-NMDAR (n=7;21%), anti-Ma2 (n=6;18%), anti-CASPR2 (n=4;12%), anti-zic4 (n=2;6%), anti-LGI1 (n=1;3%), anti-Yo (n=1;3%), anti-amphiphysin (n=1;3%), anti-recoverin(n=1;3%) and anti-SOX1(n=1;3%). Five (15%) had associated malignancy. Focal seizures with altered awareness were the most common seizure type (n=23;70%), most with either motor onset (n=13;57%) or behaviour arrest onset (n=10;43%). One third presented as refractory epilepsies. EEG was abnormal in 27 (82%) patients, 21 (64%) with paroxistic activity. Inflammatory CSF was present in 18 (55%) and nine (27%) had findings suggesting encephalitis in MRI. 22 patients (67%) were treated with immunotherapy; median time interval between first seizure and treatment was one month; preferred treatment was intravenous methylprednisolone(n=16;48%). 24 (73%) patients were seizure free at last medical visit (follow-up of 1–420 months), with only five (15%), all intracellular antibody-associated, needing more than one antiepileptic drug, and only six (18%) needing chronic immunotherapy.
Conclusion: Epilepsies associated with anti-neuronal antibody positivity may present with a mostly favourable clinical outcome.
Disclosure: Nothing to disclose.

OPR-062

Incidence of Post-Stroke Epilepsy in Denmark

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Background and aims: Stroke is a major cause of epilepsy, and more than half of epilepsies occurring after 60 years of age are caused by stroke. In this study, we investigate the incidence of post-stroke epilepsy in Denmark.
Methods: This is a nationwide register-based cohort study of all individuals who were residents in Denmark and over 18 years of age between April 1 2004 and December 31 2016. We identified all first episodes with stroke through the Danish Stroke Registry. Each stroke patient was matched with five persons without stroke on age, sex and calendar time. We excluded persons with epilepsy prior to inclusion (index date). Patients and matched persons were followed until December 31 2016, death, emigration or diagnosis of epilepsy. We calculated the incidence rate of epilepsy by severity and type of stroke (acute ischemic (AIS), or Intracerebral Hemorrhage (ICH)).
Results: The incidence rate (IR) of epilepsy was 11.4 per 10,000 person years in persons without stroke and in persons with stroke, the incidence rate of epilepsy was 123.6 per 10,000 person years (Incidence rate ratio (IRR): 10.85; 95% CI: 10.54–11.16). Compared to persons without stroke, the highest incidence of epilepsy was found among persons with very severe stroke; very severe ICH (IRR 58.27; 95% CI: 48.55–69.93) and very severe AIS (IRR 45.33; 95% CI: 40.46-–50.80). See tables

	Persons in group	Risk time (yrs)	Cases of epilepsy (n)	Incidencerate (pr 10,000 yrs)	Incidencerateratio	95% CI Low	95% CI High
Control	519054	2512085	2862	11,39	1		
Any stroke	103811	389803	4817	123,58	10,85	10,54	11,16
Control	39340	183793	226	12,30	1		
- Very severe	7868	10085	583	578,08	47,01	42,97	51,43
Control	40314	192276	245	12,74	1		
- Severe	8063	20106	713	354,61	27,83	25,65	30,19
Control	73465	351932	406	11,54	1		
- Moderate	14693	49381	860	174,15	15,10	14,05	16,22
Control	273100	1391775	1544	11,09	1		
- Mild	54620	250358	1912	76,37	6,88	6,57	7,21
Control	40380	269154	319	11,85	1		
- Unknown	8076	36845	527	142,99	12,06	11,01	13,22
Control	52455	123154	122	9,91	1		
- TCI	10491	23007	222	96,49	9,74	8,40	11,29

Incidence of epilepsy after stroke

	Persons in group	Risk time (yrs)	Cases of epilepsy (n)	Incidencerate (pr 10,000 yrs)	Incidencerateratio	95% CI Low	95% CI High
Control	368499	1806354	2098	11,61	1		
Ischemic stroke	73700	288758	3352	116,08	9,99	9,65	10,35
Control	23840	105265	131	12,44	1		
- Very severe	4768	6966	393	564,17	45,33	40,46	50,80
Control	29794	137899	176	12,76	1		
- Severe	5959	14777	544	368,14	28,84	26,23	31,72
Control	58715	271564	314	11,56	1		
- Moderate	11743	38862	640	164,68	14,24	13,10	15,49
Control	230490	1124434	1255	11,16	1		
- Mild	46098	204009	1449	71,03	6,36	6,03	6,71
Control	25660	167192	222	13,28	1		
- Unknown	5132	24144	326	135,02	10,17	9,04	11,44

Incidence of epilepsy after acute ischemic stroke

	Persons in group	Risk time (yrs)	Cases of epilepsy (n)	Incidencerate (pr 10,000 yrs)	Incidencerateratio	95% CI Low	95% CI High
Control	51630	262374	282	10,75	1		
Any ICH	10326	28061	861	306,83	28,55	26,52	30,73
Control	12925	63453	70	11,03	1		
- Very severe	2585	2505	161	642,79	58,27	48,55	69,93
Control	7835	37951	48	12,65	1		
- Severe	1567	3785	141	372,49	29,45	23,97	36,18
Control	8745	42640	47	11,02	1		
- Moderate	1749	5505	155	281,58	25,55	20,93	31,17
Control	15650	77564	82	10,57	1		
- Mild	3130	12391	284	229,21	21,68	18,84	24,94
Control	6475	40767	35	8,59	1		
- Unknown	1295	3875	120	309,64	36,07	28,51	45,62

Incidence of epilepsy after intercerebral hemorrhage

Conclusion: Risk of epilepsy after stroke is overall more than 11 times increased compared to persons without epilepsy. Severity of stroke was strongly associated with risk of epilepsy.

Disclosure: This work was supported by the Novo Nordisk Foundation (NNF16OC0019126), Health Research Foundation of Central Denmark Region, and the Danish Epilepsy Association.

OPR-063

CT perfusion to diagnose Non Convulsive Status Epilepticus in the Emergency Room

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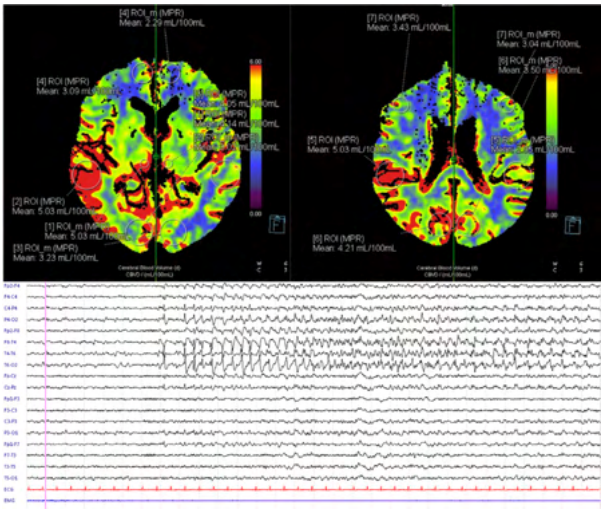
Background and aims: Failure in recognizing Nonconvulsive status epilepticus (SE) can have important negative consequences leading to diagnostic delay increasing the probability of an unfavorable prognosis. Cerebral perfusion-computed tomography (CTP) is an helpful tool for decision-making in the emergency situation. In this work we illustrate our center's experience and we evaluate the pattern of CTP in relation to Salzburg Consensus Criteria (SCC) for NCSE.

Methods: We included all NCSE studied in the ER with a CTP then confirmed by EEG and/or clinical features-evolution. All the 1st acquired EEGs for each patients were classified in accordance to SCC. CTP were evaluated either by visual inspection or by quantitative evaluation of through regions of interest (ROIs) placement and asymmetry indexes calculation.

Results: We included 21 focal NCSE. An hyper-perfusion pattern was found in 17 patients: 12 with a Definite NCSE (D-NCSE) [fig 1], two with a Possible NCSE (P-NCSE) and three with a post-ictal pattern (N-NCSE). two patients had a normo-perfusion pattern and a D-NCSE and two had an hypo-perfusion pattern and a D-NCSE. All the 10 patients (100%) presenting with continuous EEG ictal patterns showed an hyper-perfusion CTP. Eight patients presented discrete seizures: four (50%) had hyper-perfusion, two (25%) a normal perfusion study, while two (25%) had an hypo-perfusion one.



CTP showing rCBV increase in right temporo-parietal areas; EEG showing spike and wave activities at 2Hz with a temporal evolution to a delta activity at 3Hz located in the right temporo-parietal region (SCC: pattern 2c)

Conclusion: In the presence of a clinical suspicion of an epileptic event, finding hyper-perfusion CTP pattern is highly correlated to the presence of a NCSE with continuous ictal activity. CTP can speed up the diagnosis of NCSE in the emergency situation.
Disclosure: I have no disclosure to declare

OPR-184

Seizures following reperfusion treatment for stroke: multicentre, propensity score matched study

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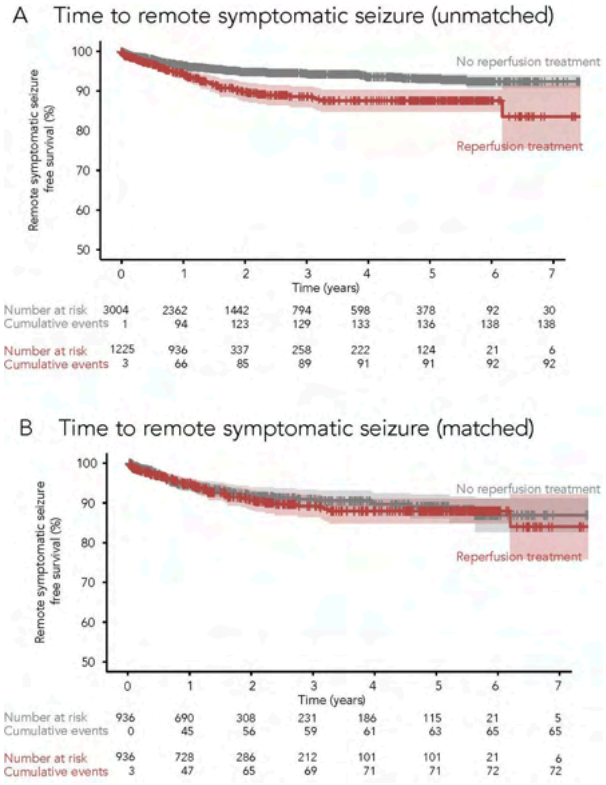
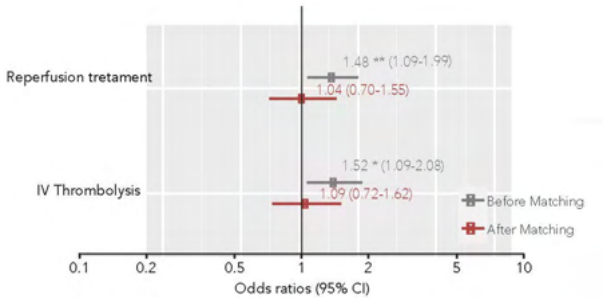
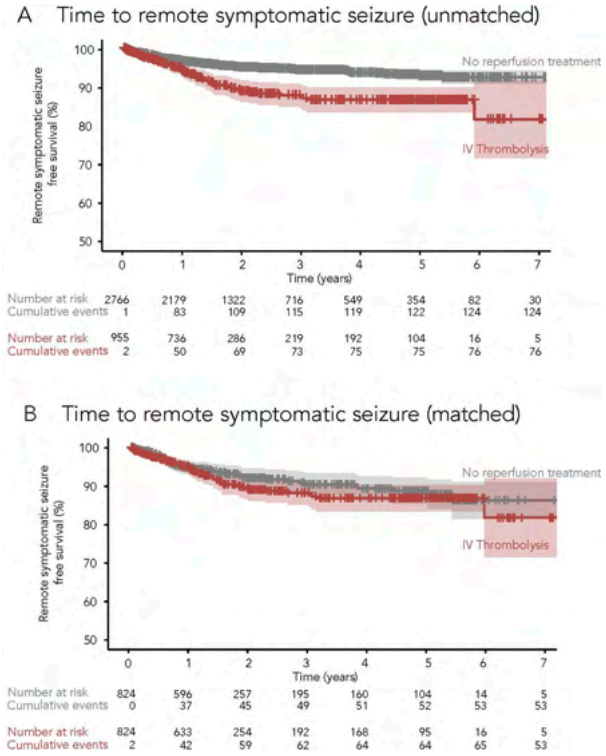
Background and aims: Reperfusion treatments are the standards of care for acute ischemic stroke. There are concerns that they increase the risk of post-stroke seizures. Here we compared the frequency of seizures after acute ischemic stroke with or without reperfusion treatments.
Methods: This multicenter study included adults from eight European referral centers with ischemic stroke and without a past history of seizures. We compared the risk of post-stroke epilepsy or acute symptomatic seizures between participants with or without reperfusion treatment using intravenous or intraarterial thrombolysis and/or mechanical thrombectomy. We used propensity score matching to reduce confounding due to treatment selection.
Results: The cohort included 4229 participants of whom 1225 (29%) had reperfusion treatment, 196 (5%) experienced acute symptomatic seizures, and 232 (6%) had post-stroke epilepsy. Median follow up time was 1.6 years (interquartile range 1.0–3.3). After matching (n=936 in each group), there was no association between reperfusion treatment and time to post-stroke epilepsy (hazard ratio [HR] 1.05, 95% confidence interval [CI] 0.75–1.48, p=0.74) or risk of acute symptomatic seizures (odds ratio [OR] 1.04, 95% CI 0.70–1.55, p=0.84). In a matched secondary analysis (n=824 in each group), there was no association between receiving intravenous thrombolysis and time to post-stroke epilepsy (HR 1.15, 95% CI 0.80–1.65, p=0.43) and risk of acute symptomatic seizures (OR 1.08, 95% CI 0.72–1.62, p=0.68).



Kaplan-Meier estimates of time to post-stroke epilepsy after acute ischemic stroke (A) before and (B) after matching for the propensity to receive or not reperfusion treatment. Time at baseline was index stroke. Shaded bands represent 95% CI



Forest plot showing odd ratios and 95% confidence intervals (horizontal lines) for the risk of acute symptomatic seizures after acute ischemic stroke.



Kaplan-Meier estimates of time to post-stroke epilepsy after acute ischemic stroke (A) before and (B) after matching for the propensity to receive or not IV thrombolysis. Time at baseline was index stroke. Shaded bands represent 95% confidence interval.

Conclusion: We did not find an association of reperfusion treatment after ischemic stroke with the risk of acute symptomatic seizures or post-stroke epilepsy.
Disclosure: Nothing to disclose.

OPR-196

Autistic traits and language impairment in children of women with epilepsy are not mediated by unmetabolized folic acid

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Background and aims: Pregnant women with epilepsy using folic acid (FA) supplements may accumulate unmetabolized folic acid (UMFA) in plasma. We examined the effect of UMFA concentrations in pregnancy on autistic traits and language impairment risk in children of women with epilepsy.

Methods: We included 227 children of 203 women with epilepsy on antiseizure medication (ASM) enrolled in the Norwegian Mother, Father and Child Cohort Study (MoBa). Plasma folate and UMFA concentrations were measured in gestational weeks 17–19. Data on ASM use, FA supplement, and autistic traits and language impairment at age 1.5–8 years were collected from parent-reported questionnaires.

Results: In 208 of 227 children, the mothers reported use of FA supplements between gestational weeks -4 to 20. FA dose data were available for 76 children, in 58 of these, high-dose FA intake (1 mg or more) was reported. High maternal folate concentrations correlated with high UMFA concentrations (n=227, Spearman's rho=0.66, p-value<0.001), but not with FA dose (n=76, Spearman's rho=0.21, p-value=0.06). The UMFA concentrations did not differ between children with and without autistic traits and language impairment at any age. Linear regression analyses adjusted for covariates, showed no association between the UMFA concentrations and autistic traits and language scores.

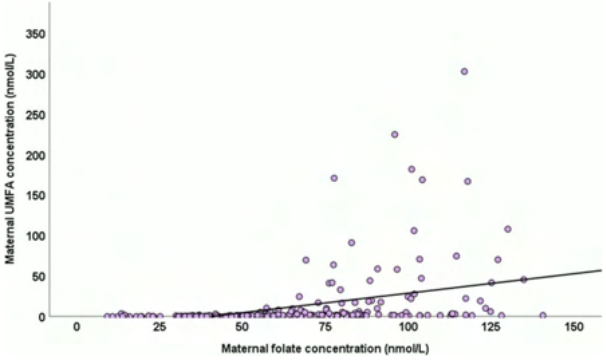

Figure 1; Scatter plot of unmetabolized folic acid (UMFA) concentration and folate concentration measured in maternal plasma in gestational weeks 17–19

		n	Detected UMFA n (%)	Maternal UMFA (nmol/L) *mean, median (range)*	p-value[c]
Child autistic traits at different ages[a]					
3 years	YES	9	8 (89)	18.8, 3.45 (74.7)	0.272
	NO	110	90 (82)	16.6, 1.32 (303.0)	
8 years	YES	1	1 (100)	91.1, 91.1 (0.00)	0.072
	NO	82	64 (78)	12.8, 1.31 (169.0)	
Child language impairment at different ages[b]					
1.5 years	YES	26	21 (81)	9.1, 1.2 (58.8)	0.733
	NO	124	100 (81)	15.7, 1.3 (303)	
3 years	YES	12	8 (67)	3.7, 1.2 (17.1)	0.255
	NO	110	92 (84)	17.8, 1.5 (303)	
5 years	YES	24	18 (75)	8.0, 1.6 (44.2)	0.732
	NO	58	51 (88)	15.5, 1.7 (182.0)	
8 years	YES	26	19 (73)	10.7, 1.7 (91.1)	0.973
	NO	58	47 (81)	14.9, 1.2 (169.0)	

ASM, antiseizure medication. UMFA, unmetabolized folic acid.
[a]Autistic traits at 3 and 8 years according to the Social Communication Questionnaire (SCQ). [b]Language delay at 1.5 years according to the Ages and Stages Questionnaire (ASQ), at 3 years according to the ASQ and one question on expressive language delay, at 5 years according to the ASQ, Twenty Statements about Langue-related Difficulties (Language 20) and the Speech and Language Assessment Scale (SLAS), and at 8 years according to the Language 20 [c]The Mann-Whitney U test for continuous variables was used due to violation of the assumption of normal distribution

Table 1: The pregnancy unmetabolized folic acid (UMFA) concentration in children of women with epilepsy with autistic traits or language impairment at ages 1.5–8 years, respectively, compared to children without autistic traits or language impairment.

		Score interpretation	B	SE B	β[a]	p-value	95% CI
Autistic traits							
3 years	(SCQ)	Lower is normal	-0.013	0.009	-0.135	0.159	-0.031-0.005
8 years	(SCQ)	Lower is normal	0.005	0.011	0.056	0.638	-0.016-0.026
Language impairment							
1.5 years	(ASQ)	Higher is normal	0.013	0.019	0.060	0.489	-0.024-0.050
3 years	(EL)	Higher is normal	0.001	0.002	0.045	0.642	-0.003-0.004
3 years	(ASQ)	Higher is normal	0.007	0.013	0.050	0.606	-0.020-0.034
5 years	(ASQ)	Higher is normal	0.004	0.018	0.026	0.835	-0.032-0.040
5 years	(SLAS)	Higher is normal	0.000	0.002	-0.013	0.915	-0.004-0.004
5 years	(Lang 20)	Lower is normal	-0.014	0.028	-0.063	0.602	-0.070-0.041
8 years	(Lang 20)	Lower is normal	-0.006	0.016	-0.046	0.698	-0.038-0.026

UMFA, unmetabolized folic acid. B, unstandardized beta. β, standardized beta. SE, standard error. SCQ, the Social Communication Questionnaire. ASQ, the Ages and Stages Questionnaire. SLAS, the Speech and Language Assessment Scale. EL, one question on expressive language delay. Lang20, Twenty Statements about Language-related Difficulties. N may vary slightly in the adjusted model due to missing data.
[a]Variables in the adjusted model: maternal age, any AED concentrations (standardized), topiramate use yes/no, SES (single mother or low education or low household income), symptoms of anxiety and/or depression during pregnancy. If the variables SES, maternal depression, smoking and maternal age did not change the β with more than a change in the third decimal, they were not included in the final model

Table 2: The association between maternal plasma UMFA concentration and the autistic trait scores and language scores at ages 1.5–8 years, respectively, adjusted for relevant covariates.

Conclusion: We found no association between UMFA concentrations during pregnancy and risk of autistic traits or language impairment in children of women with epilepsy on ASM. Our study does not support any harmful effect of UMFA on brain development in foetal life, supporting that high-dose FA is safe for ASM-treated women with epilepsy in pregnancy.

Disclosure: There are no relevant disclosures regarding this study.

OPR-197

Progressive DNA methylation reprogramming of neuroinflammatory processes in epilepsy

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Background and aims: Neuroinflammation is an established epileptogenesis hallmark. Exacerbated pro-inflammation has been widely described in epileptic brain, being, in fact, associated with seizure causative effects. Mesial Temporal Lobe Epilepsy (MTLE) patients often suffer from Hippocampal Sclerosis (HS), a pattern of histopathological damage characterized by severe neuronal cell loss and enhanced gliosis. Epigenetic regulatory mechanisms have been proposed to contribute for epiletogenesis onset and progression through the establishment of altered transcriptomic patterns. DNA methylation, a modulator of chromatin structure and accessibility linked to gene expression repression, is considered a prominent player in the unveiling of the ethiopathogenic mechanisms of epilepsy.
Methods: Hippocampal DNA methylation profiling was performed with Infinium HumanMethylationEPIC BeachChips in eight MTLE-HS patients subjected to resective surgery. DNA methylation values were correlated with epilepsy duration (years) using Spearman's correlation ($rho>0.5$; $p<0.01$).
Results: We observed 2,601 and 3,104 CpGs whose methylation in the hippocampus correlated inversely and positively with epilepsy duration, respectively. Gene ontology analysis of both clusters showed enrichment of multiple inflammatory terms, with emphasis for MHC and peptide antigen binding. Binding-motif enrichment demonstrated overrepresentation of transcription factors involved in inflammation. We highlighted interferon regulatory factor 1 (IRF1), a known proponent of the disease-associated microglia phenotype.
Conclusion: Epileptogenesis is not static, with increased seizure frequency and severity being regularly observed. DNA methylation is here described has a potential modulator of pro-inflammatory neurodegeneration coupled with epilepsy progression. Special attention must be given to the role of microglia in this landscape.
Disclosure: R.M.-F. attends the Biomedical Sciences doctoral programme at Institute of Biomedical Sciences Abel Salazar of University of Porto, funded by FCT (Fundação para a Ciência e Tecnologia) fellowship (grant number SFRH/BD/137900/2018).

Multiple Sclerosis: Observational and real-life studies

OPR-188

Cardiovascular risk factors affect brain volume in young multiple sclerosis patients

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Background and aims: We aimed to investigate impact of cardiovascular risk factors (CV-RF) on brain atrophy in multiple sclerosis (MS) patients aged 50, given results for older patients may be confounded by small vessel disease.
Methods: Study included 124 (79 relapsing-remitting, 45 progressive) MS patients (age 36±8, range 18–50), and 95 healthy controls (HC) (age 35±8, range 18–50). Subjects underwent brain 3T MRI with sequences for assessing lesions and atrophy. Traditional CV-RF (smoking5pack-years, presence of hypertension, dyslipidemia, diabetes/prediabetes) were assessed, including more stringent cut-offs (smoking10pack-years, treatment for above conditions). Linear models adjusted for age, sex, disease duration, phenotype and treatment were used to determine the impact of CV-RF on MRI variables.
Results: Nineteen HC and 48 MS patients had one traditional CV-RF, four HC and 15 MS patients had >1. Ten HC and 30 MS patients had one stringent CV-RF, three and eight had >1. In MS patients, the presence of two traditional CV-RF was associated with reduced normalized grey matter volume (NGMV) (p=0.01), white matter volume (NWMV) (p=0.03) and brain volume (NBV) (p=0.003), and not with T2-lesion volume (T2-LV) (p=0.27). In MS patients, the presence of one stringent CV-RF was associated with reduced NGMV (p=0.006), NWMV (p=0.003) and NBV (p<0.001), and higher T2-LV (p=0.03). In HC, no differences were observed according to either traditional or stringent CV-RF presence.
Conclusion: The presence of CV-RF is associated with brain atrophy in MS patients, even under age 50. CV-RF seem to have synergistic effects, determining brain atrophy even for levels of exposure when present in combination.
Disclosure: Partially supported by grants from Fondazione Italiana Sclerosi Multipla (FISM/2018/R/16).

OPR-189

Safety analysis of offspring breastfed by mothers on glatiramer acetate therapy for relapsing multiple sclerosis

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Background and aims: Prescribing labels for most relapsing multiple sclerosis (RMS) disease-modifying therapies (DMTs), including glatiramer acetate (GA), advise against use during breastfeeding. Limited clinical safety data exist for offspring who are breastfed by mothers receiving GA.
Methods: This non-interventional, retrospective analysis used data from the national German MS and Pregnancy Registry (January 2011–January 2020). Eligible participants had a RMS diagnosis, pregnancy resulting in live birth, and received either Copaxone® (GA; 20 or 40 mg/mL) or no DMT while breastfeeding.
Results: Overall, 60 offspring from the GA cohort (59 pregnancies; 58 women) and 60 from the control (60 pregnancies; 60 women) were included. Maternal demographics and RMS prognostic factors were descriptively comparable in both (Table 1). "Cumulative" GA-exposure was higher in the GA cohort vs control, because 86.7% of the offspring's mothers received GA during pregnancy (vs 25%). Safety outcomes ≤18 months postpartum (Table 2) showed offspring hospitalisation frequency and incidence were similar between cohorts. Frequency of annualised hospitalisation events were slightly lower in offspring in the GA cohort (0.20 [confidence interval {CI}=0.09–0.31]) vs the control (0.25 [CI=0.12–0.38]). Frequency and incidence of antibiotic use were similar between cohorts. Growth parameters (body weight, body length and head circumference) were also comparable. Paediatrician check-ups at 12 months identified 3 (2.5%; N=120 [CI=0.52–7.13]) offspring with developmental delays; were in the control cohort (n=60; 5% [CI=1.04–13.92]).

Table 1: Demographic and baseline characteristic data for breastfeeding women with RMS analysed in the COBRA study

	GA-exposed cohort* (n=58)	Unexposed cohort (n=60)
Patient demographics		
Mean (SD) age at the time of conception, years	33.1 (3.3)	32.9 (3.6)
Mean (SD) BMI at the beginning of pregnancy	25.1 (5.6)	24.5 (5.7)†
Median (range) follow-up duration, months	13.3 (1.1–42.6)	24.7 (0.3–49.1)
Disease activity		
Mean (SD) disease duration at conception, years	4.6 (4.0)	6.8 (5.1)
Median (range) number of relapses in the 2 years preceding conception	1.0 (0.0–5.0)	1.0 (0.0–6.0)
Median (range) number of relapses during pregnancy	0.0 (0.0–2.0)	0.0 (0.0–2.0)
Median (range) number of steroid pulses during pregnancy	0.0 (0.0–2.0)	0.0 (0.0–1.0)
Pregnancy/breastfeeding		
Median (range) gestational week of pregnancies at entry into the German Multiple Sclerosis and Pregnancy Registry	11.3 (1.0–39.3)	7.8 (3.6–38.3)
Number (%) of infants born preterm‡	3.0 (5.0)	3.0 (5.0)
Number (%) of infants who were exclusively breastfed‡	47.0 (78.3)	49.0 (81.7)
Median (range) duration of breastfeeding, months	7.9 (0.2–22.4)	8.1 (0.2–28.2)
GA exposure		
Number (%) of infants exposed to GA during pregnancy‡	52.0 (86.7)	15.0 (25.0)
Median (range) duration of GA exposure during pregnancy, days	66.0 (21.0–291.0)	29.0 (6.0–41.0)
Median (range) duration of GA-exposed breastfeeding, months	7.0 (0.2–19.1)	NA

BMI, body mass index; GA, glatiramer acetate; NA, not applicable; SD, standard deviation
*One woman gave birth to twins (n=58 women; n=59 pregnancies; n=60 infants)
†n=58
‡Based on the number of infants (n=60)

Table 2: Safety outcomes for all enroled infants for the period of 12-months postpartum

	GA-exposed (n=60)	Unexposed (n=60)
Hospitalisation (frequency)		
Number of events	12	15
Annualised number of events (95% CI)	0.20 (0.09–0.31)	0.25 (0.12–0.38)
Hospitalisation (incidence)		
Number of infants with an event	11	12
Proportion of population with an event (95% CI)	18.33 (9.52–30.44)	20.00 (10.78–32.33)
Antibiotic treatments (frequency)		
Number of events	13	10
Annualised number of events (95% CI)	0.22 (0.10–0.33)	0.17 (0.06–0.27)
Antibiotic treatments (incidence)		
Number of infants with an event	9	9
Proportion of population with an event (95% CI)	15.00 (7.10–26.57)	15.00 (7.10–26.57)
Diagnosed developmental delays at 12 months postpartum		
Number of infants with an event	0	3
Proportion of population with an event (95% CI)	0.00 (0.00–5.96)	5.00 (1.04–13.92)
Body measurements at 10–12 months postpartum	**GA-exposed (n=50)**	**Unexposed (n=51)**
Mean body weight, grams	9636.20	9549.22
Mean body length, cm	75.27	76.30
Mean head circumference, cm	46.07	46.21

CI, confidence interval; GA, glatiramer acetate
GA-exposed=infants breastfed by mothers exposed to GA during lactation; unexposed=infants breastfed by mothers not exposed to any disease-modifying therapy during lactation; overall=both infant cohorts combined

Conclusion: No evidence was found that maternal GA exposure during breastfeeding adversely affected the offspring's body measurements, incidences of developmental delay, and frequency and incidences of hospitalisations or antibiotic treatment use.

Disclosure: A.I.C. has received speaker honoraria from Bayer Healthcare and travel grants from Sanofi Genzyme, Teva and Novartis.

OPR-190

Comparison of the 2017 and 2010 revisions of the McDonald criteria CIS patients: a multicentre MAGNIMS study

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Background and aims: In 2017, a revision of the 2010 McDonald criteria for multiple sclerosis (MS) diagnosis in clinically isolated syndrome (CIS) was proposed. We compared the performance of 2017 and 2010 McDonald criteria in predicting MS development and anticipating MS diagnosis.

Methods: Brain and spinal cord MRI and cerebrospinal fluid (CSF) examination obtained at CIS onset and a follow-up brain MRI acquired 15 months from CIS onset were assessed in 785 CIS patients from nine European centres. Performances of the 2017 and 2010 McDonald criteria for dissemination in space (DIS), time (DIT) and DIS+DIT, also including oligoclonal bands (OCBs) assessment, in predicting a second clinical attack (clinically-definite [CD] MS), and median time to MS diagnosis were evaluated.

Results: At follow-up (median=69.1 months), 406/785 CIS patients (52%) developed CDMS. At month-36, the 2017 DIS criteria had higher sensitivity (0.86 vs 0.78), lower specificity (0.32 vs 0.38), and similar area under the curve (AUC, 0.59 vs 0.58). The 2017 DIS+DIT criteria had higher sensitivity (0.74 vs 0.66), lower specificity (0.54 vs 0.60), and similar AUC (0.64 vs 0.63). OCB assessment increased sensitivity (0.83), decreased specificity (0.39), preserving AUC (0.61). MS diagnosis was earlier with the 2017 vs the 2010 or CDMS criteria, especially with OCB assessment (2017 revision with/without OCBs=3.2/11.4 months; 2010 revision=13.0 months; CDMS=58.5 months).

Conclusion: The 2017 vs 2010 McDonald criteria showed higher sensitivity, lower specificity, and similar accuracy in predicting CDMS. They simplify the clinical use of MRI criteria, allowing an earlier MS diagnosis without reducing accuracy.

Disclosure: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

OPR-191

Observational study on real-life experience with alemtuzumab in naïve patients with aggressive Multiple Sclerosis

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Background and aims: Alemtuzumab(ALEM) is an anti-CD52 monoclonal antibody for the treatment of active Multiple Sclerosis(MS) which showed high efficacy also in the subgroup of highly-active patients. We aimed to evaluate efficacy/safety profile of ALEM-treatment in a population of aggressive MS naïve-patients

Methods: We conducted a multicenter prospective observational study in a cohort of aggressive naïve-patients treated with ALEM. Clinical and neuroradiological parameters were collected from clinical records in 27 Italian MS Centers from October 2015 to September 2020

Results: 133 naïve patients were included. Basal characteristics are shown in Table1. Efficacy data were analyzed after the end of the complete therapeutic cycle (two ALEM-courses) because presence of disease activity between the two courses is not indicative of a therapeutic failure. Follow-up data at 24 and 36 months were available for 99/133 and 61/133 subjects, respectively. NEDA-3 at 24 and 36 months was reached by 89,2% and 69,4% of patients, respectively. At 24 and 36 months mean ARR were 0,06 and 0,1; median EDSS were 2,0 and 1,5, respectively. At the same time-points, mean increase in T2 lesions was 0,2 and 0,48 respectively. 5,3% of patients needed a third cycle of therapy. Overall 74,4% of patients reported adverse events (Table2)

Table 1. Basal Characteristics	
Number of patients included	133
Age at treatment, mean ± SD	31.4 ± 8.9
Sex: Females - Males, n(%)	F: 80 (60.2) – M: 53 (39.8)
Time to treatment from disease onset (months), median (IQR)	8 (4 – 27)
Follow-up in months, mean ± SD	34.2 (12.1)
Baseline EDSS, median (IQ range)	3.0 (2.0 – 3.5)
ARR previous year, mean ± SD	1.8 ± 0.9
Number of Brain T2-hyperintense lesions at MRI baseline, mean ± SD	29.8 ± 20.8
Number of brain Gd+ lesions at MRI baseline, mean ± SD	3.4 ± 5.1
Number of spinal cord T2/STIR-hyperintense lesions at MRI baseline, mean ± SD	5.0 ± 3.0
Number of spinal cord Gd+ lesions at MRI baseline, mean ± SD	0.9 ± 1.5

Table 1

Table 2. Adverse events	
Any AEs	99 (74.4%)
Infusion-associated reactions (IARs)	94 (70.1%)
Autoimmune AEs	23 (17.3%)
Thyroid dysfunction	21 (15.8%)
Immune thrombocytopenia (ITP)	1 (0.8%)
Other autoimmune AEs	2 (1.5%)
Infectious AEs	13 (9.8%)
Urinary tract infections (UTI)	4 (3.0%)
Pneumonia	4 (3.0%)
VZV reactivation	2 (1.5%)
CMV reactivation	1 (0.8%)
Listeriosis	2 (1.5%)
Other infectious AEs	1 (0.8%)

Table 2

Conclusion: These results highlight that aggressive naïve-patients are an ideal candidate for immune system resetting, likely due to young age, short disease duration and low disability. Furthermore, absence of previous immuno-modulating/immunosuppressant drugs altering the immune system play a key role in determining effectiveness of this powerful drug. Longer FU is needed to confirm our data

Disclosure: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors

OPR-192

Comparable efficacy of natalizumab EID and SID on neuroperformance measures in RRMS: real-world evidence from MS PATHS

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Background and aims: Natalizumab extended interval dosing (EID) is associated with lower progressive multifocal leukoencephalopathy risk than standard interval dosing (SID) in anti–JC virus antibody positive multiple sclerosis patients. However, EID efficacy has yet to be demonstrated in a randomised controlled trial, and real-world efficacy data would be valuable.

Methods: This study compared Multiple Sclerosis Performance Test (MSPT) functional changes occurring during treatment with natalizumab EID versus SID in MS PATHS, a network of healthcare institutions providing access to real-world clinical data. An MSPT segment was defined as the time between two MSPT assessments six months apart. MSPT segments with average infusion cycles >35 days and 35 days were defined as EID and SID, respectively. Patients could contribute multiple segments to both groups. Missing covariate data were multiply imputed. Covariates at segment start (Table) were balanced between groups by inverse probability weighting (IPW) based on a logistic propensity score model. Differences in annualized change in MSPT scores were compared between EID/SID arms with weighted linear regression.

Table. Covariates at start of EID and SID MSPT segments in MSPATHS

Baseline Characteristic	EID (n=152)[a]	SID (n=1079)[a]
Natalizumab treatment duration, mean (SD), y	4.74 (3.39)	3.88 (2.98)
Age, mean (SD), y	43.36 (11.24)	43.18 (10.27)
Sex, n (%)		
Female	110 (72.4)	828 (76.7)
Male	48 (31.6)	251 (23.3)
Race, n (%)		
Black/African American	19 (12.5)	152 (14.1)
White	120 (78.9)	872 (80.8)
Other	13 (8.6)	55 (5.1)
Education, mean (SD), y	14.61 (2.33)	15.08 (2.51)
MS duration, mean (SD), y	11.88 (7.40)	10.48 (7.49)
PDDS, mean (SD)	2.09 (1.98)	1.76 (1.95)
Relapses prior to segment, mean (SD)	0.39 (0.70)	0.43 (0.81)
PST z score, mean (SD)	−0.62 (1.32)	−0.35 (1.25)
MDT z score, mean (SD)	−1.14 (1.69)	−0.59 (1.77)
WST z score, mean (SD)	−1.84 (3.02)	−1.44 (4.13)

[a]n=number of MSPT segments. The EID and SID arms had 88 and 387 unique patients, respectively.
MDT, manual dexterity test; MS, multiple sclerosis; MSPT, Multiple Sclerosis Performance Test; PDDS, Patient Determined Disease Steps; PST, processing speed test; SD, standard deviation; WST, walking speed test.

Table. Covariates at start of EID and SID MSPT segments in MSPATHS

Results: Data from 152 EID and 1,079 SID segments were analysed. After IPW, all baseline factors exhibited a standard mean difference 0.05. Annualised change in MSPT scores of processing speed, manual dexterity, and ambulation did not differ significantly between EID and SID. On average, MSPT scores were maintained or improved while on natalizumab (Figure).

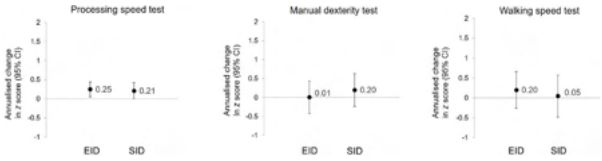

Figure. Annualised change in z score for each neuroperformance measure in the EID and SID arms

Conclusion: Functional outcomes between patients treated with natalizumab EID versus SID were comparable. Cognitive processing speed, manual dexterity, and walking speed were maintained or improved over time for both treatment groups.

Disclosure: This study is supported by Biogen.

OPR-193

Exit-strategy in Natalizumab responders RRMS patients: an Italian comparison among Ocrelizumab, Rituximab and Cladribine

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Background and aims: The long exposure to Natalizumab (NTZ) treatment and anti-JC virus (JCV) seropositivity expose patients to a higher risk to develop progressive multifocal leukoencephalopathy (PML),
Methods: A multicentre, retrospective, real-world study on consecutive RRMS patients from eleven tertiary Italian MS centres, who switched from NTZ to OCR, RTX and CLA from January 1st, 2018 to December 31st, 2019. The primary study outcome was the annualized relapse rate (ARR) after 18 months on the investigated drugs. Treatment effects were estimated by the inverse probability weighting (IPW) generalized linear regression model for ARR. Additional endpoints included 24 and 48 weeks confirmed disability progression (CDP) as measured by Expanded Disability Status Scale and Magnetic Resonance Imaging activity after 12 months. Adverse events (AEs) were also collected.
Results: Patients fulfilling the required criteria were 120. Out of them, 64 switched to OCR, 36 to RTX and 20 to CLA. Patients from the three groups did not shown differences for baseline characteristics, also after post-hoc analysis. The generalized linear regression model adjusted for IPW revealed that patients on OCR had a lower risk for ARR than patients on CLA (ExpB OCR 0.485, CI 95% 0.264–0.893, p=0.020). No differences were found in other pairwise comparisons (OCR vs RTX and RTX vs CLA). AEs rates were similar among the three groups.
Conclusion: Conclusions: OCR revealed to better control early disease activity compared to CLA. All the DMTs investigated were safe. Further data are needed.
Disclosure: Nothing to disclose.

ePresentations

Saturday, June 19 2021
Ageing and dementia 1

EPR-001

Brain architecture changes across the FTLD spectrum

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Background and aims: To explore structural/functional MRI connectomic features of the motor neuron disease (MND) and behavioral variant of frontotemporal dementia (bvFTD) spectrum.
Methods: 115 MND (including amyotrophic lateral sclerosis [ALS] and primary lateral sclerosis), 35 bvFTD patients and 61 controls underwent clinical/cognitive and MRI evaluations. MND patients were divided in 79 pure-motor (MND-motor) and 36 cognitive/behavioral impaired (MND-ci/bi). A sub-analysis was performed on ALS patients only (54 ALS-motor, 21 ALS-ci/bi and eight ALS-FTD). Graph analysis and connectomics assessed structural/functional topological network properties at global, lobar and regional level.
Results: Globally, bvFTD showed altered structural and functional network properties compared to all other groups. At lobar level, bvFTD showed altered structural and functional network properties within the frontotemporal and basal ganglia areas relative to all groups. Structural alterations in the parietal lobe discriminated bvFTD from controls and MND-motor only. MND groups showed altered structural properties within sensorimotor and basal ganglia areas relative to controls. Regionally, bvFTD showed widespread structural damage and decreased functional connectivity relative to all groups. MND showed disrupted structural architecture and enhanced functional connectivity within sensorimotor, basal ganglia and frontotemporal areas relative to controls. Similar results have been found in ALS sub-analysis.
Conclusion: The disruption of the structural architecture in MND worsens in relation with cognitive deficits. Functional changes are characterized by enhanced functional connectivity in presence of exclusive motor impairment that intensifies with the occurrence of cognitive impairment in MND.
Disclosure: The Italian Ministry of Health (GR-2011-02351217; GR-2013-02357415; RF-2011-02351193) and riSLA (ConnectALS).

EPR-002

Stepwise connectivity paves the way to functional network vulnerability in age-related neurodegenerative disorders

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Background and aims: Ageing is the main risk factor for most neurodegenerative diseases and results in complex transformations of the human brain function. The aim of this study was to investigate how topological organization of the brain connectome changes with age using resting-state functional MRI and stepwise functional connectivity (SFC) analyses.
Methods: 138 controls were recruited and divided into two groups according to age: 55 young (20–30 years [YC]) and 83 old (41–84 years [OC]). SFC analysis aims to characterize regions that connect to specific seed brain areas at different levels of link-step distances. Eight well-known hubs of the human connectome were selected as seeds: middle frontal gyrus, rostral anterior and posterior cingulate cortex, precuneus, inferior parietal, middle temporal and lingual gyri and pericalcarine cortex. Whole-brain 2-sample t-test comparisons between groups were performed.
Results: At 1-link step distance, in OC, all the seed regions displayed decreased regional–local functional connectivity with superior frontal and medial orbital frontal gyri, rostral anterior and isthmus cingulate cortex, precuneus and middle and inferior temporal gyri relative to YC; across intermediate link-steps, a reduced connectivity was observed between all seed regions and frontal-parietal lobes. By contrast, at the 1st link-step distance, YC showed lower connectivity only between few seed regions and precentral, paracentral and lateral occipital gyri compared to OC. At intermediate link-step distances, increased connectivity with sensorimotor regions was found in OC relative to YC.
Conclusion: SFC approach might have important implication providing a starting point for evaluating network disruptions in age-related neurodegenerative disorders.
Disclosure: European Research Council (StG-2016_714388_NeuroTRACK).

EPR-003

Cognitive assessment and EEG as first-line screening tools for neuroprotection trials in prodromal synucleinopathy

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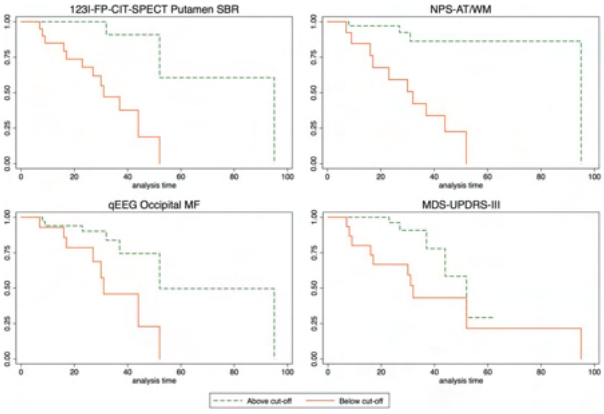
Background and aims: Dopamine transporter (DAT) SPECT is the strongest risk factor for phenoconversion in patients with idiopathic REM sleep behavior disorder (iRBD). However, it is not widely available. Aim of the study is to investigate whether other cost-effective and widely available biomarkers may be used as first-line screening tools.

Methods: 47 consecutive iRBD patients (68.53±7.16 yo, 40 males) underwent baseline clinical assessment, olfaction testing, comprehensive neuropsychological evaluation, resting EEG and DAT-SPECT. All patients underwent six month-based clinical follow-up to investigate the emergence of parkinsonism and/or dementia. Survival analysis and Cox regression were used to estimate conversion risk.

Results: 17 patients developed an overt synucleinopathy (8 parkinsonism and nine dementia) 32.8±22 months after diagnosis. The strongest risk factors were putamen specific to non-displaceable binding ratios (SBR) (HR 7.3, 95% confidence interval, CI 1.8–29.4), attention/working memory cognitive function (NPS-AT/WM) (HR 5.9, 95% CI 1.8–19.7), EEG occipital mean frequency (MF) (HR 2.7, 95% CI 1.0–7.7) and clinical motor assessment (MDS-UPDRS-III) (HR 2.3, 95% CI 0.8–6.2) (Figure 1). On multivariate Cox regression analysis, putamen SBR, NPS-AT/WM and occipital MF significantly contributed to the model (HR 11.3, 95% CI 2.5–50.3), while the model with NPS-AT/WM and occipital MF was weaker but still highly significant (HR 6.2, 95% CI 1.9–19.8).



Kaplan-Meier disease-free survival plot of iRBD patients according to the best predictors of phenoconversion. Red solid lines indicate patients below cut-off while green dashed lines indicate patients above cut-off, for each feature.

Conclusion: DAT-SPECT is confirmed as the strongest phenoconversion risk factor for iRBD patients. However, comprehensive neuropsychological assessment and resting EEG can be useful, cost-effective and widely available first-line screening tools, to be used to select patients that deserve DAT-SPECT as 2nd-line screening tool for neuroprotective clinical trials.

Disclosure: Nothing to disclose.

EPR-004

Montreal Cognitive Assessment as a predictor of Mild Cognitive Impairment risk of conversion to Dementia

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Background and aims: Mild cognitive impairment (MCI) is considered a prodromal state of dementia. Abnormal values of cerebrospinal fluid (CSF) biomarkers (amyloid-b1-42 (A42), total tau (t-tau) and phosphorylated tau (p-tau)) have been associated with higher risk of conversion from MCI to dementia. Studies evaluating Montreal Cognitive Assessment's (MoCA) ability in this task are lacking. This study aims to investigate the relationship between MoCA and CSF biomarkers, as well as the ability of those instruments to predict conversion to dementia.
Methods: We retrospectively studied our cohort of MCI with a longitudinal systematic follow-up. We investigated the correlation of MoCA with all the biological variables. We further examined the role of MoCA in conversion risk using Kaplan-Meier and Cox regression models. ROC curves were also calculated for the most relevant variables and conversion at 24 months.
Results: We included 236 MCI patients. During follow-up (mean=20.9 months), 40.3% of the patients converted to dementia. MoCA scores were correlated with all CSF biomarkers. Higher age of onset, ApoE-4, lower MoCA, decreased A42 and increased t-tau and p-tau were associated with increased risk of conversion. A42 and MoCA were independent predictors of conversion.
Conclusion: This study shows the utility of MoCA in predicting conversion to dementia, especially in patients with a higher level of education, supporting its use in the evaluation of MCI patients.
Disclosure: No disclosures.

EPR-005

Task-Free functional networks related to emotion processing in frontotemporal lobar degeneration

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Background and aims: To investigate the relationship between emotion processing and resting-state functional connectivity (RS-FC) in frontotemporal lobar degeneration (FTLD).
Methods: 80 FTLD patients and 65 age-matched healthy controls underwent brain 3.0 Tesla MRI [3DT1-weighted and RS-functional MRI (RS-fMRI)] and neuropsychological assessment, including the Comprehensive Affect Testing System (CATS). FLAME models in FSL were performed between each emotion construct and RS-FC changes within crucial networks.
Results: FTLD patients performed worse than controls in all CATS-subtests. In controls, a high performance at the emotion naming and emotion matching constructs was related with increased RS-FC within the cerebellar network, and a high performance at the emotion discrimination construct was related with increased RS-FC of the right occipital face area (OFA) within the visuo-associative network. In FTLD patients, high performances at the emotion naming construct were related with increased RS-FC of the bilateral OFA within the visuo-associative network and the bilateral frontal pole within the default-mode-network, whereas high performances at the emotion matching construct were related with increased RS-FC of the left OFA within the visuo-associative network. Finally, in FTLD patients, high performances at each emotional construct were related with decreased RS-FC within the basal ganglia network.
Conclusion: In healthy controls and FTLD patients, the RS-FC within crucial networks is related to different constructs of emotion processing. In FTLD, the RS-FC associated with emotional performances involved a large number of brain regions, likely due to brain functional specificity loss and compensatory attempts. These findings offer potential markers for detecting functional vulnerability linked to social interactions.
Disclosure: Supported by the Italian Ministry of Health (GR-2013-02357415); European Research Council (StG-2016_714388_NeuroTRACK).

EPR-006

A multiparametric MRI study of structural brain damage in dementia with Lewy bodies: comparison with Alzheimer's disease

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Background and aims: To investigate gray (GM) and white matter (WM) damage in patients with dementia with Lewy bodies (DLB) compared to those with Alzheimer's disease (AD).
Methods: 24 DLB patients, 26 age- and disease severity-matched AD patients, and 20 age and sex-matched healthy controls performed clinical and neuropsychological assessment, and brain structural and diffusion tensor (DT) MRI. GM atrophy was investigated using voxel-based morphometry, WM hyperintensities (WMHs) using a local thresholding segmentation technique, and normal appearing WM damage using tract-based spatial statistic.
Results: DLB and AD patients were at a mild-to-moderate stage of dementia. Compared to controls, AD patients showed a widespread pattern of GM damage, while DLB cases had GM atrophy involving bilateral thalamus and temporal regions. Compared to DLB, AD patients exhibited GM atrophy in bilateral fronto-temporal and occipital regions. Both DLB and AD patients presented with higher WMH load than controls, with no differences among each other. WMHs in DLB were diffuse with relative prevalence in posterior parietal-occipital regions. Compared to controls, both DLB and AD patients showed reduced microstructural integrity of the main supratentorial and infratentorial WM tracts. WM microstructural damage of posterior regions was more severe in AD than DLB patients.
Conclusion: DLB showed prominent WM degeneration compared to the limited GM atrophy, while in AD both tissue compartments were severely involved. In DLB, WM microstructural degeneration was independent of WMHs, thus revealing two possible underlying processes. Different pathophysiological mechanisms are likely to drive GM and WM damage distribution in DLB and AD.
Disclosure: This study was partially supported by the Italian Ministry of Health (grant #GR-2011-02351217).

EPR-007

Mathematical modeling reveals the correlates of cognitive impairment across the FTLD spectrum

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Background and aims: . Amyotrophic lateral sclerosis (ALS), and behavioral variant frontotemporal dementia (bvFTD) lie on a continuum. The study aim was to apply mathematical modeling to unravel MRI connectomic signatures of cognitive/behavioral impairment in ALS.
Methods: 83 ALS, 35 bvFTD and 61 controls underwent clinical/cognitive evaluations and MRI scan. Neuropsychological testing identified 54 ALS with only motor deficits (ALS-motor), 21 ALS with cognitive/behavioral impairment (ALS-ci/bi) and eight ALS with bvFTD (ALS-FTD). Structural and functional connectivity values were considered and normalized relative to controls. Statistical distribution analysis was performed between patient groups.
Results: Compared to ALS-motor, bvFTD showed greater structural disruption within and between frontal, temporal and parietal lobes. Conversely, ALS-motor showed a greater damage within sensorimotor–basal ganglia connections relative to bvFTD. ALS-ci/bi and ALS-FTD showed an ALS-like pattern within motor areas, whereas a bvFTD-like pattern was found only within the parietotemporal connections in ALS-ci/bi and within frontal and frontal-sensorimotor connections in ALS-FTD. Functionally, bvFTD showed decreased functional connectivity in frontotemporal and sensorimotor-parietal connections compared to ALS-motor. ALS-ci/bi showed enhanced functional connectivity relative to bvFTD in the frontal-sensorimotor, parietotemporal connections and within sensorimotor areas, while ALS-FTD showed reduced functional connectivity in temporal-sensorimotor connections compared to ALS subgroups.
Conclusion: Two characteristic patterns were identified: alterations of the frontotemporal and parietal networks as bvFTD-like, and a more focal damage within sensorimotor-basal ganglia areas as ALS-like, bringing to light features that ALS-ci/bi and ALS-FTD shared with the twoends of ALS-bvFTD spectrum.
Disclosure: The Italian Ministry of Health (GR-2011-02351217; GR-2013-02357415; RF-2011-02351193) and AriSLA (ConnectALS).

Autonomic nervous system diseases

EPR-008

Comparison of baroreflex sensitivity indices with standard tests of autonomic nervous system function

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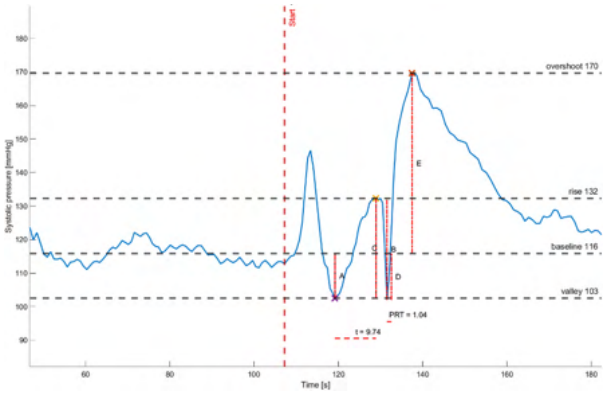
Background and aims: In order to further evaluate clinical usefulness of - and -adrenergic components of the baroreflex sensitivity (BRS) index, the aim of this study was to compare them to standardized measures of autonomic dysfunction.

Methods: In 275 participants (mean age 40.57±15.19, range 18 to 89 years, 76.4% females) referred for testing of the autonomic nervous system, -BRSa, -BRSa and BRSv were compared (Fig. 1.) to heart rate (HR) and blood pressure (BP) values, adrenergic and cardiovagal indices of the Composite Autonomic Severity Score and heart rate



variability (HRV) parameters.
Figure 1. An example of -BRSa, -BRSa and BRSv calculation.

Results: -BRSa showed statistically significant positive correlation with all HR and BP parameters in supine position and negative with adrenergic index. -BRSa showed statistically significant positive correlation with the adrenergic index. BRSv showed statistically significant negative correlation with all HR and BP parameters and all HRV parameters. In a univariable logistic regression model, -BRSa was a negative predictor (Exp(B) 0.866, 95% CI 0.782–0.959, p=0.006, respectively) of pathological adrenergic index. To differentiate between subjects with normal and pathological adrenergic index, the optimal cutoff for -BRSa was found to be 6.741, which gave a sensitivity of 61.0% and a specificity of 56.0% (Fig. 2).

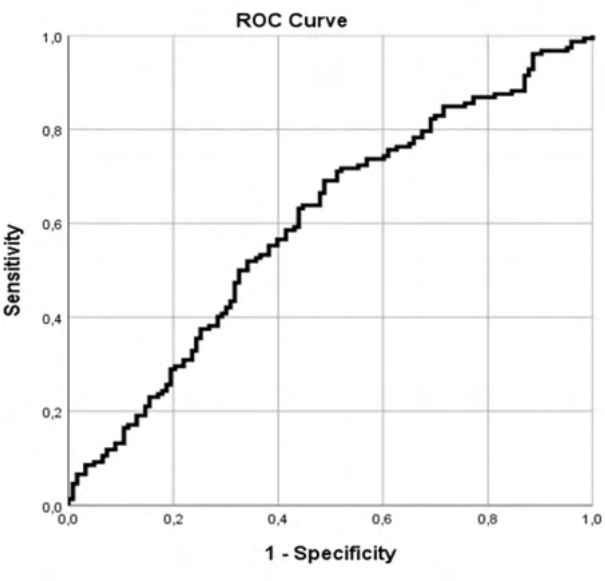


Figure 2. Sensitivity and specificity of -BRSa to differentiate between subjects with normal and pathological adrenergic index.

Conclusion: BRSa indices showed a good correlation with standard measures of ANS function, -BRSa performed well as a adrenergic receptors mediated sympathetic nervous system marker, while -BRSa had a very low sensitivity in discriminating patients with or without sympathetic dysfunction.

Disclosure: No relevant disclosures.

EPR-009

Autonomic responses to concert performance: a scientific divertissement

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Background and aims: Music Performance Anxiety (MPA) is the experience of marked nervousness related to musical performance which worsens the quality of musical execution and can be treated using Biofeedback in multimodal therapy. The aim of this is study is to evaluate the autonomic responses to performing a piano concert.
Methods: Nine professional pianists participated in the study. We recorded electrocardiographic RR-intervals and beat to beat systolic and diastolic blood pressures (BPsys, Bpdia), at four time points: baseline at rest, during warm-up and during and after a concert performance. The played piece was Prelude op. Nine number 1 by Alexander Scriabin, written for the left hand. We calculated parameters of sympathetic cardiac modulation (RRI-low-frequency-powers) and parasympathetic cardiac modulation (RRI-high-frequency-powers) by wavelet analysis. We compared parameters between the four time points [ANOVA or Friedman test with post-hoc analysis].
Results: During the concert performance compared to baseline, there was a significant decrease in RR-intervals (i.e. increase in heart rate) (89.67±10.05 vs 104.19±9.44 bpm, $p<0.05$), a significant increase in BPsys (122.17±6.73 vs 146.13±13.81mmHg, $p<0.05$) and BPdia (75.47±2.78 vs 86.89±5.67mmHg, $p<0.05$), a significant increase in sympathetic RRI-low-frequency-powers (79.00±5.43 vs 88.21± 3.29, $p<0.05$) and a decrease in parasympathetic RRI-high-frequency-powers (21.00±5.43 vs 11,29, $p<0.05$).
Conclusion: The increase in sympathetic cardiac autonomic modulation during the concert reflects the MPA that musician experience. In order to reduce MPA, heart rate variability by wavelet analysis could be used as Biofeedback in multimodal therapy.
Disclosure: Nothing to disclose.

EPR-010

Relationship between brainstem atrophy and autonomic failure in Multiple systemic Atrophy

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Background and aims: Multiple-System atrophy (MSA) is characterized by a severe autonomic failure considered as essentially of central origin. The aim of this study is to investigate the relationship between different autonomic parameters and brainsteam atrophy.
Methods: Analysis of patients who have had: Cerebral MRI, severity disease assessment (UMSARS) score and explorations of the autonomic nervous system (ANS) assessment (SCOPA-AUT scale, heart rate variability (HRV) and, blood pressure (BP) variations during the Ewing tests (Deep breathing, tilt test, Valsalva, hand grip), and sweat response (Sudoscan)). T1-3D MRI scans were analysed by automated segmentation (FreeSurfer 7.0 software). Uni and multivariate analysis were performed to study the association between ANS parameters of dysautonomy and volumes of the brainstem, putamens and cerebellum.
Results: 89 patients were included (age 68±8 years, 73% MSA Probable, 70% MSA-P). MRI were performed 1±1.2 years after diagnosis. No significant association was found between ANS parameters and brainsteam atrophy . Atrophy of the brainsteam, putamens and cerebellar grey matter was associated with a lower supine systolic BP. Atrophy of the cerebellar white matter (CWM) and of the putamens was associated with a decreased systolic BP during the Valsalva maneuver and during the tilt test, respectively.
Conclusion: This study showed that impaired sympathetic cardiovascular response was associated with atrophy of putamens and CWM. Studies using advanced MRI approaches are needed to clarify changes in brainsteam structures associated with autonomic failure in AMS.
Disclosure: Nothing to disclose.

EPR-011

Short- and long-term effects of siponimod on heart rate variability in people with secondary progressive MS

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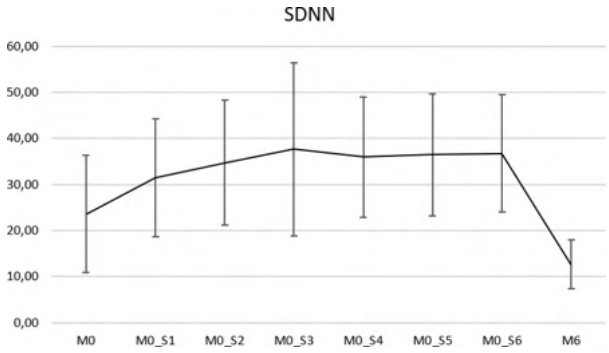
Background and aims: The aim of this study was determine the short- and long-term effects of siponimod on heart rate variability (HRV) in people with secondary progressive multiple sclerosis (pwSPMS).

Methods: In 26 pwSPMS (16 females, mean age 50.96±9.48, median EDSS 6.0, range 3.0–6.5) HRV analysis was performed for the: a) 10 minutes interval in the supine position prior to treatment initiation (M0), b) average values for the six 30-min intervals in the period of three hours after treatment initiation (M0s1–6), and 10 minutes interval in the supine position after at least six months of treatment with siponimod (M6). The following HRV parameters were used for analysis: high-frequency (expressed in normalized units - HFnu) and low frequency (expressed in absolute units - LF) power of RR intervals, LF to HF ratio (LF/HF) and standard deviation of NN intervals (SDNN).



SDDN values before, three hours and six months after ingestion of siponimod.

Results: In all six intervals after siponimod ingestion (M0s1-6), SDNN, LF, and LF/HF showed higher and HFnu lower values compared to M0 (M0s6 SDNN 36.461±12.26, LF 826.997±638.619, HFnu 30.658±12.208 vs M0 SDNN 22.981±12.519, LF 312.284±343.513, HFnu 41.236±14.738, all p<0.001.). After six months of continuous treatment with siponimod, SDNN and LF showed significantly lower values compared to M0 (M6 SDNN 12.597±5.291, LF 65.549±49.399 vs M0 SDNN 23.589±12.745 (Figure 1), LF 326.724±353.298 all p0.001.), while no difference was observed for HFnu.

Conclusion: In the short-term, siponimod causes a significant increase in HRV 3h after the first intake. In the long-term, six months after continuous treatment, a significant decrease in HRV is seen.

Disclosure: MH: Participated as a clinical investigator and/or received consultation and/or speaker fees from: Biogen, Sanofi Genzyme, Merck, Bayer, Novartis, Pliva/Teva, Roche, Alvogen, Actelion, Alexion Pharmaceuticals, TG Pharmaceuticals.

EPR-012

Log-term effects of siponimod on ANS function in people with secondary progressive MS

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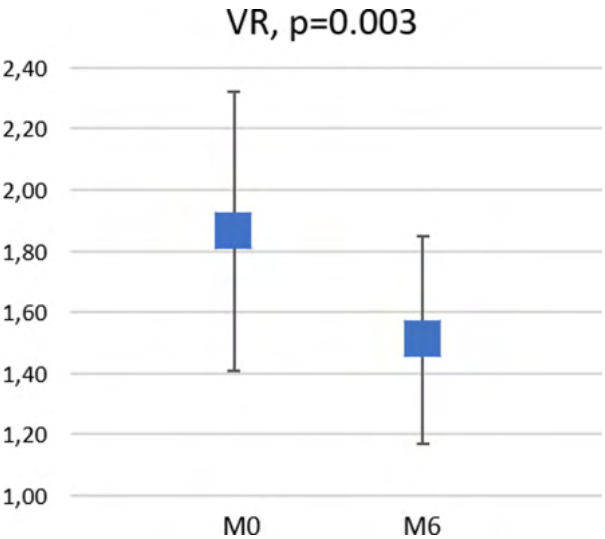
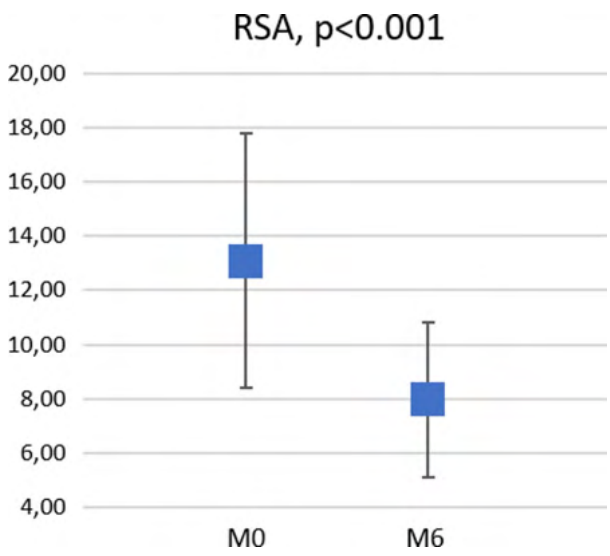
Background and aims: The aim of this study was to determine the long-term effects of siponimod on autonomic nervous system (ANS) function in people with secondary progressive multiple sclerosis (pwSPMS).

Methods: Out of 26 pwMS in whom treatment with siponimod was initiated, 24 completed at least six months of continuous therapy (2 patients discontinued treatment due to side-effects), (15 females, mean age 51.25±8.69, median EDSS 6.0, range 3.0–6.5). The following ANS tests were performed before (M0) and after six months of treatment (M6): 10-min supine resting position, Valsalva maneuver, deep breathing test and 10 min tilt-up table test. The severity and distribution of ANS function was quantitated using adrenergic and cardiovagal indices of the Composite Autonomic Severity Scale (CASS).

Results: At M6, Valsalva ratio and respiratory sinus arrhythmia were lower compared to M0 values (1.510±0.338 vs 1.864±0.456, p=0.003 and 7.969±2.865 vs 13.091±4.687, p<0.001, respectively) (Figures 1, 2). Cardiovagal index was significantly higher at M6 compared to M0 (1 (range 0–2) vs 0 (range 0–1), p=0.008, respectively). At M0, three patients had orthostatic hypotension and none had orthostatic hypertension. At M6, five patients had orthostatic hypotension and three had orthostatic hypertension. There was no difference in adrenergic index between M6 and M0 (0 (range 0–3) vs 0 (range 0–3), p=0.114, respectively). At M6, a blunted response of heart rate to tilt was observed compared to M0 (9±7 vs 14±9, p<0.001).



Comparison of Valsalva ratio (VR) at M0 and M6



Comparions of respiratory sinus arrhythmia (RSA) at M0 and M6

Conclusion: This study has shown significant worsening of tests that measure parasympathetic nervous system function in pwSPMS after six months of treatment with siponimod.
Disclosure: Nothing to disclose.

Cerebrovascular diseases 1

EPR-013

Abstract withdrawn

EPR-014

Primary angiitis of the central nervous system: the path to a challenging diagnosis

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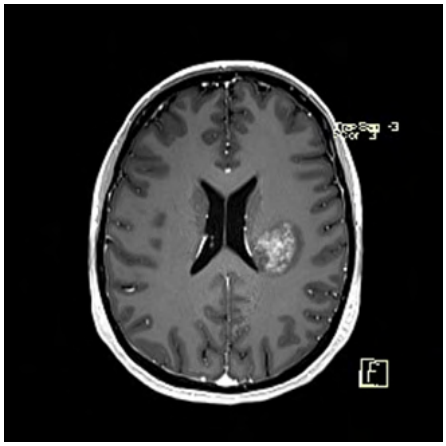
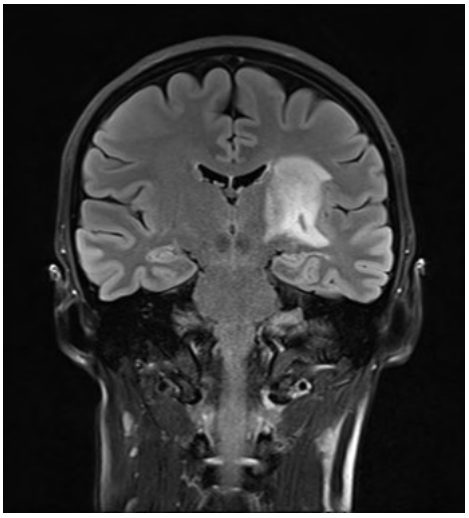
Background and aims: Primary angiitis of the central nervous system is a rare life-threatening vasculitis, with an annual incidence of 2.4 cases per million, accounting for just 1% of all vasculitides. It has a variable radiological appearance, requiring a high diagnostic suspicion index. While typical multifocal, we report a case presenting with a solitary parenchymal brain lesion, debuting in the first trimester of pregnancy.
Methods: A 38-year old pregnant woman without any medical history, developed progressive right hemibody sensorimotor deficit, in the absence of headache. Imaging revealed a non-homogenous, contrast enhanced, cortico-subcortical left frontal lesion, with diffusion restriction and intralesional SWI-negative spots. MR-angiography was normal. Biological assessment was negative for autoimmunity markers and infectious agents (including VZV), ruling out systemic involvement. Brain biopsy revealed lymphocytes infiltrating intraluminal and perivascular spaces within the white matter, suggestive for lymphocytic vasculitis with necrotic foci. Immunohistochemistry highlights Ki67+ CD45+ T-Lymphocytes. Demyelination and glial tumoral proliferation were excluded. Rare Ki67- B-Lymphocytes excluded an intravascular lymphoma. Also there was no detection of in-situ EBV.

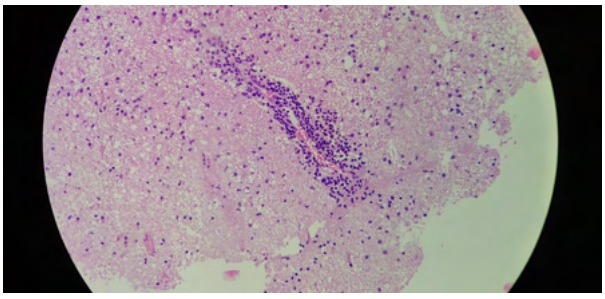


Contrast enhanced axial brain MRI sequence showing enhancing parenchymal focal lesion



Coronal Flair image showing cortico-subcortical left frontal lesion

Results: Induction monotherapy with high-dose intravenous glucocorticoids was initially unsuccessful, so monthly intravenous cyclophosphamide pulses (750 mg/m2) were started. After three courses, the Modified Rankin Scale improved from four to 2. Brain MRI confirmed the clinical improvement, showing lesion size and contrast enhancement reduction. At six months, as remission was achieved, cyclophosphamide was stopped and mycophenolate mofetil was chosen for maintenance therapy.
Conclusion: This case highlights one of the many faces of a rare entity, posing a significant diagnostic challenge and prompting early recognition and aggressive treatment.



Brain biopsy showing intraluminal and perivascular lymphocytic infiltrate (hematoxylin & eosin staining)

Disclosure: Nothing to disclose.

EPR-015

Increased cerebrovascular reactivity during spontaneous migraine attacks

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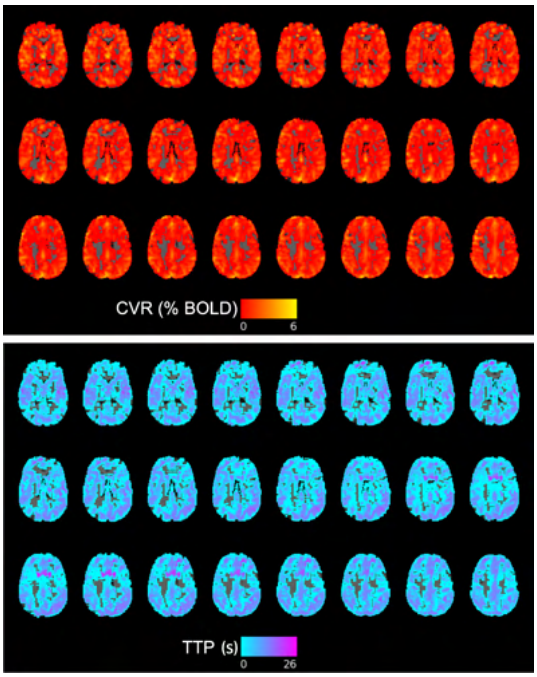
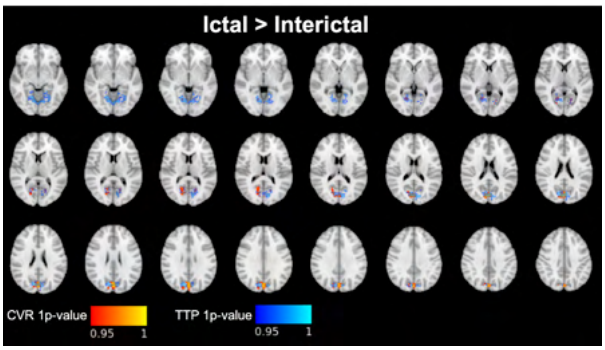
Background and aims: Migraine is a disabling neurological condition, characterized by intermittent headache attacks (ictal phase) alternating with pain-free (interictal) periods, which is associated with a 2-fold increased risk of ischemic stroke. Cerebrovascular reactivity (CVR) studies with transcranial Doppler (TCD) have shown differences between ictal and interictal phases of migraine, as well as between migraineurs and controls. We used BOLD-fMRI with breath-holding (BH) to measure CVR during both migraine phases. In contrast to TCD, fMRI allows measurements across the whole brain, and with high spatial resolution, and can thus be used to further explore possible microvascular differences in the cerebral pathophysiology of migraineurs.

Methods: 11 female patients (36±7yrs) with episodic migraine without aura were studied on two sessions: during ictal and interictal phases. BOLD-fMRI data were acquired during a BH task (3 cycles of 20s BH alternated with normal breathing). The amplitude (CVR, percent signal change) and time-to-peak (TTP) of the BH BOLD response were computed. Group-level analysis was performed to identify differences in CVR and TTP between ictal and interictal phases.

Results: Representative CVR and TTP maps are shown in Fig.1. Group-analysis revealed increased CVR and TTP in occipital regions during the attack compared with the interictal phase (Fig.2).



Representative CVR (top) and TTP (bottom) maps of one illustrative subject.



Group-level analysis: maps of statistically significant differences between the ictal and interictal phases. Increased CVR and TTP were found in the ictal vs. interictal phase in occipital regions ($p<0.05$, corrected for multiple comparisons).

Conclusion: This result is consistent with reported reduced reactivity of the posterior cerebral circulation in the interictal phase of migraineurs relative to controls using TCD. Impaired interictal CVR in occipital regions may indicate an endothelium dysfunction, possibly suggesting an increased risk of ischemic stroke during this phase of migraine.

Disclosure: Nothing to disclose

EPR-016

Dissecting Aneurysms Of Internal Carotid And Vertebral Arteries: Clinical And Angiographic Follow-Up

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Background and aims: To study clinical and angiographic follow up of dissecting aneurysms (DA) of internal carotid (ICA) and vertebral arteries (VA).
Methods: We examined 289 patients with ICA/VA dissection verified by neuroimaging. Clinical follow-up lasted 5,7±3,8 years, during which 10 patients received anticoagulants, 18 – antiplatelet drugs. Eight patients were without antithrombotic drugs (AT), three patients successfully underwent stenting. The last repeated angiography was performed in 3,2±3,9 year.
Results: DA was found in 36 patients (12%) (women, 58%, mean age -37,8±10,1 years): ICA – 21 patients, VA – 15. The DA size was less 10mm (19), more 10mm (17). There were no recurrent ischemic attacks during follow-up. On repeated angiography DA size was the same (13), increased by 7,3±8,7mm (3) or decreased (1). 13 small DA disappeared. The comparison of patients with and without DA showed that the former more often had multiple dissections (38% vs 20%, p=0.022), whereas artery lumen occlusion in the acute period was less frequent (14% vs 42%, p=0.001). The latter pointed to intramural hematoma (IMH) spreading to adventitia, rather than its subintimal localization.
Conclusion: The frequency of ICA/VA DA is 12%. Their development is facilitated by a more pronounced the arterial wall weakness (multiple dissections, a tendency of IMH spreading to adventitia). DA, appears, to have a benign course and is not a source of embolism. It seems no clear indications for AT drugs to prevent ischemic recurrence. Indications for stenting are relative, given the favorable clinical course.
Disclosure: Nothing to disclose

EPR-017

Neutrophil Extracellular Traps (NETs) in Human Cerebral Thrombi of different Stroke Etiology

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Background and aims: Inflammation is emerging as an essential trigger of thrombosis and neutrophils have been demonstrated to promote thrombus formation. Indeed, different timing, site and thrombotic elements involved in clot constitution might account for diverse neutrophil activation and NETosis pattern (cellular, filopodia, and web-like) among diverse embolic sources. We here aimed to unravel the histopathological composition of cerebral thrombi, with a focus on neutrophils and NETs.
Methods: We performed a systematic histological analysis of 80 cerebral human thrombi retrieved by endovascular thrombectomy (EVT) in acute ischemic stroke patients. We investigated clot composition, in terms of neutrophils (MPO+ cells) and NETs (CitH3+ area). The prevalent morphological features of NETs (cell-dominant, filopodia-dominant, or web-dominant) were visually assessed by three independent investigators.
Results: Neutrophils and NETs were largely represented within cerebral thrombi. NET percentage was found to be higher in cardioembolic compared to atherosclerotic clots (p=0.04). The association between NETs content and stroke etiology remained significant after adjusted analysis (beta coefficient=-6.19, 95%CI=-11.69 to-1.34, p=0.01). The predominant NETs morphological feature was similar among diverse stroke etiologies (p=0.27). Compared to CE, LAA thrombi showed a higher proportion - although not statistically significant – of cell-dominant pattern (LAA:36.4%, n=4. CE:16.7%, n=7).
Conclusion: NETs represent an important component of human cerebral thrombi and their amount and morphological features seem to reflect different underlying stroke pathogenetic mechanisms. Although a clear signature to identify stroke etiology by thrombus evaluation has still to be defined, the analysis of thrombus composition might represent a challenge in understanding the diverse thrombo-inflammatory mechanisms underlying stroke etiology.
Disclosure: Nothing to disclose

EPR-018

Headache at onset of first-ever ischemic stroke

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Background and aims: No studies have prospectively investigated headache at onset of first-ever ischemic stroke, along with a large concurrent control group. Our aims were to answer twoimportant questions: 1) are headaches at stroke onset causally related to the stroke and what are their typical clinical characteristics? 2) what aetiology of stroke is associated with these headaches?

Methods: The study population consisted of 550 patients (mean age 63,1, 54% males) with 1st-ever ischemic stroke, and 192 control patients (mean age 58.7, 36% males) admitted to the emergency room without any acute neurological deficits or serious disorders. All data were collected prospectively, using a standardized case-report form during face-to-face interviews by neurologists.

Results: Headache at onset of ischemic stroke was present in 82 (14.9%) of 550 patients. More than half (56%) had a new type of headache (mainly migraine-like) simultaneously with stroke onset, and 36% had headache with altered characteristics (mainly tension-type headache). Headaches were associated with cardioembolism (p=0.002, OR 2.4; 95% CI 1.4–4.1), posterior circulation stroke (p=0.01, OR 2.0; 95% CI 1.2–3.5), infarcts >15mm (p=0.03; 95% CI 1.1.–2.7), infarcts of the cerebellum (p=0.02, OR 2.3; 95% CI 1.1–4.8), good neurological status (p=0.01, OR 2.5; 95% CI 1.2–4.9) and a low frequency large-artery atherosclerosis (p=0.004, OR 0.4; 95% CI 0,2–0,8).

Conclusion: At stroke onset, headache of a new type, and headache with altered characteristics, were related to ischemic stroke. They were associated with certain aetiologies of stroke.

Disclosure: No disclosures.

EPR-019

Temporal Trends of Functional Outcome in Acute Stroke Patients Treated with Intravenous Thrombolysis

M. Marko [1], D. Miksova [2], A. Langer [1], J. Ebner [1], P. Sommer [3], W. Serles [1], M. Knoflach [4], W. Lang [5], S. Kiechl [4], S. Greisenegger [6]

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Background and aims: Intravenous thrombolysis with recombinant tissue plasminogen activator (rtPA) is an established treatment for patients with acute ischemic stroke and substantially improves functional outcome. Since its implementation into clinical routine there has been an increase in rtPA-treatment; we aim to assess whether there is an associated increase in good functional outcome over time in rtPA-treated patients.

Methods: We analyzed patient-data during the time period of 2006–2019 in the Austrian Stroke Unit Registry, a nationwide quality-of-care registry. Patients treated with rtPA and complete follow-up data at three months were included. Frequencies of good functional outcome defined as a modified Rankin Scale (mRS) score 0–2 were assessed for the overall population and prespecified subgroups.

Results: From 2006 to 2019 a total of 9396 patients were treated with rtPA and had available data on outcome at three months. Frequencies of good functional outcome increased from 45.9% in 2006 to 57.0% in 2019 in the overall population of rtPA-treated patients. We observed a more pronounced increase in good functional outcome over time in patients >70 years, patients with unknown time of symptom onset (including wake-up strokes) and patients without atrial fibrillation. Notably, good functional outcome post stroke occurred less frequent in women compared to men throughout the whole study period.

Conclusion: With increasing use of rtPA for the treatment of acute ischemic stroke there has also been an overall increase in good functional outcome over time. However, specific subgroups are still less likely to achieve good outcome and deserve particular attention in acute stroke care.

Disclosure: No disclosures.

EPR-020

Cervicocephalic arterial dissection: clinical characterization, treatment, and prognosis

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Background and aims: Cervicocephalic arterial dissection (CCAD) is the most frequent cause of stroke in young adults.
Methods: Retrospective characterization of the clinical course, therapy and prognosis of a sample of patients with CCAD between 01/2015–06/2020 in a tertiary centre.
Results: We identified 91 patients with CCAD (mean age: 48years; male: 64%). CCAD was found in the anterior circulation in 69%. Extracranial dissection was exclusively observed in half of the cases while 36% had extracranial/intracranial commitment. Previous history of trauma and headache was found in 14% and 40% of cases, respectively. Headache was present in 52% (33% as 1st symptom). Two thirds of patients had ischemic stroke symptoms. Recurrent neurologic symptoms were reported by 23% and persistent headache (>3 months) by 31%. Posterior circulation CCAD (vs anterior circulation CCAD) had more often persistent headache (53% vs. 22%; p=0.017). Angio-CT was the first study to raise the suspicion of CCAD (53%), followed by angio-MRI (48%). Cervical/Transcranial ultrasonography was the most used method for follow-up (39%). Almost 90% (75/91) of patients were treated with antiplatelet drugs (median: twoyears), whilst 17% with anticoagulation therapy. Vessel recanalization occurred in 25% of our sample (median: five months). Death occurred in 5%.
Conclusion: Most of the dissections were extracranial and in the anterior circulation. Headache was a very common symptom in the acute phase; noteworthy, it was also very frequent as a persistent complaint after posterior CCAD. Angio-CT and angio-MRI were the most commonly used methods to confirm CCAD. Recanalization was observed in only ¼ of our sample.
Disclosure: No disclosures.

Epilepsy 1

EPR-021

Convolutional network analysis for interictal EEG discrimination between subjects with epileptic seizures and PNES

M. Ascoli [1], G. Varone [2], M. Lo Giudice [2], S. Gasparini [2], V. Cianci [3], G. Mastroianni [4], G. Tripodi [1], R. Ieracitano [1], F. Vazzana [1], A. Prestandrea [1], C. Paleologo [1], S. Neri [1], V. Bova [1], A. Mammì [1], C. Ieracitano [5], F. Morabito [5], U. Aguglia [4], E. Ferlazzo [6]

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Background and aims: The differential diagnosis between epileptic seizures (ES) and psychogenic nonepileptic seizures (PNES) may be difficult, due to the lack of reliable and distinctive clinical features. Interictal EEG may also be normal in patients with ES. The gold standard for diagnosis of PNES is the video-EEG recording of a typical episode but this may be difficult to obtain and poses ethical problems. Innovative tools such as non-linear EEG analysis with the use of neural networks could provide important diagnostic support.

Methods: 18 patients with ES (12 males, six females) and 18 patients with video-EEG recorded PNES (2 males, 16 females). All included subjects had normal interictal EEG. None was taking psychotropic drugs. A 2-dimensional convolutional neural network (2D-CNN) scheme was utilized to classify the two categories of subjects (ES vs. PNES). The proposed architecture performs a feature engineering step (EEG time-frequency transformation and extraction of multiple features) and a classification step with a 2D-CNN.

Results: The developed 2D-CNN classified the EEG recordings of ES vs. PNES subjects with a fair reliability. Average accuracy was 91.25% (SD 11.39), average precision 93.75% (SD 16.53), F-measure 89.88% (SD 14.20) and recall 90.63% (SD 17.40%).

Conclusion: These preliminary data on a small sample of subjects encourage the use of these innovative diagnostic techniques. EEG-based neural network learning are promising tools for accurate differential diagnosis between ES and PNES.

Disclosure: The authors have no conflicts of interest to declare. All co-authors have seen and agree with the contents of the manuscript and there is no financial interest to report.

EPR-022

Long term thalamic recordings with Video-EEG in a patient with refractory epilepsy treated with DBS

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Background and aims: Deep Brain Stimulation (DBS) in the Anterior Nucleus of the Thalamus (ANT) is an approved therapy for drug refractory focal epilepsy. Chronic Local Field Potentials (LFP) recorded in ANT using a novel Implantable NeuroStimulator (INS, Percept™, Medtronic plc.) were compared with simultaneously recorded Video-EEG. This enabled the comparison of intra- and extra-cranial signals and aimed at identifying a patient and epilepsy type specific biomarker, which may be used in optimizing DBS for epilepsy therapy.

Methods: Using the already implanted INS enabled simultaneous bilateral DBS stimulation and intracranial recording of LFP from DBS contacts in and around ANT. The patient experienced 50% reduction of the number of seizures, occurring mainly during sleep. The INS acquired LFP with a sampling frequency of 250 Hz, converts LFP epochs of 500ms to the frequency domain and calculates the power (Pband) in a selected frequency bandwidth of interest. The average Pband over 10min is stored in the INS and is used to visualize a "timeline".

Results: 13 seizures were recorded during 48 hours of continuous recording. Figures 1 and 2 show Pband "timelines. We will present whether Pband peaks can be reliably used as a chronic seizure detector algorithm in this patient.

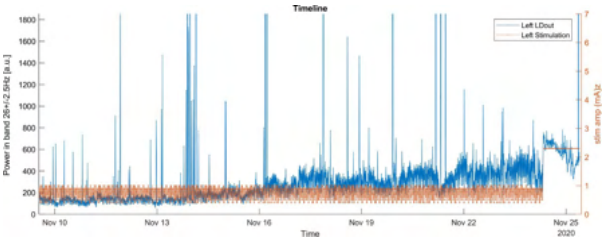

Figure 1: Two Week Timeline recording. The Pband (26±2.5 Hz) (left ANT blue line); peaks reflecting seizures in this patient. Average DBS stimulation amplitude (red line) Except the last day the stimulation was cycling: 1 min ON and five min OFF

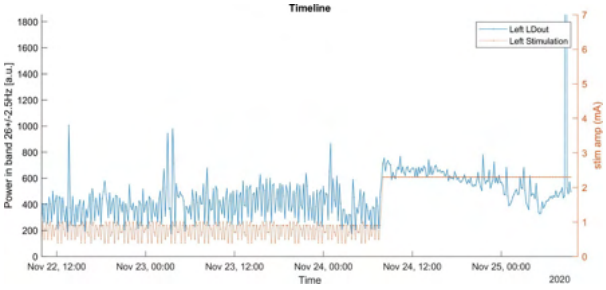

Figure 2. The last three days of Timeline recordings shown in figure 1. Video-EEG recordings are available for the last two days, and are used to study the correlation between Percept and Video-EEG recordings Last day stimulation was continuously ON

Conclusion: Seizures were identified in the LFP and were represented by Pband peaks. More recordings with different patients are needed to learn whether there is a universal epilepsy biomarker or multiple patient-specific biomarkers will be necessary for further enhancing the DBS for epilepsy therapy

Disclosure: Nothing to disclose

EPR-023

Task-based fMRI: using a clinical paradigm to predict verbal memory lateralization

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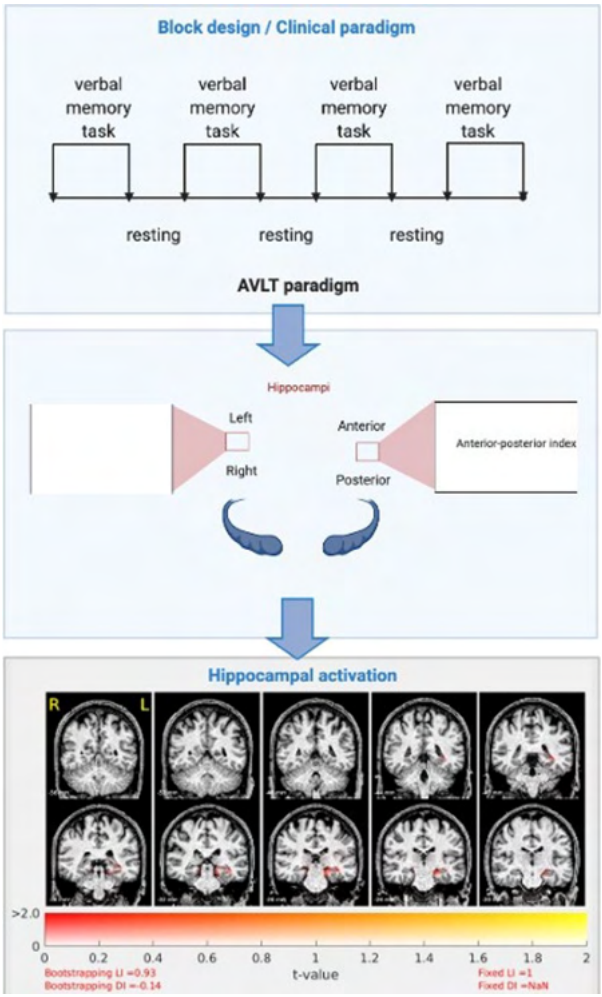
Background and aims: Functional MRI (fMRI) was introduced as a promising non-invasive tool for predicting postsurgical deficits in the presurgical evaluation of patients with pharmacoresistant epilepsy. We aim to assess fMRI power to correctly lateralize verbal memory.

Methods: 50 consecutive patients with temporal lobe epilepsy (40 left; 25 females) who underwent an fMRI memory encoding paradigm of words based on the auditory verbal learning test. We calculated the individual lateralization index of verbal memory by using bootstrapping and an anterior-posterior index along with the hippocampus. Activations with other clinical and neuropsychological parameters as a predictor of verbal memory outcome were compared.



Results: 50 patients with TLE [40 left (25 females); median age 31 years (IQR: 43–27)] and HC (32.75) (45.08–25.92) (p=0.75) with no significant age differences among. Verbal memory activation in left hippocampus was significantly higher activated in RTLE compared to HC (t:-2.46 (29), p=0.02), while not significantly different in LTLE. No activation was displayed for the left hippocampus during both the combined encoding-retrieval task in eight patients (16.3%), 7(87.5%) of them with left TLE, and five HC (22.7%). For the right hippocampus, activation was not displayed in six patients (12.2%), and eight HC (36.4%). The Sensitivity of the is 83.3% with and specificity of 50% .

Conclusion: Memory fMRI may be clinically relevant if we find a proper method for hippocampal activation. Memory fMRI shows potential clinical benefits and its development may be crucial for verbal memory lateralization prediction.

Disclosure: No disclosures.

EPR-024

Optical control of excitatory transmission in hippocampal slices with photoactive adenosine A1 receptor agonist

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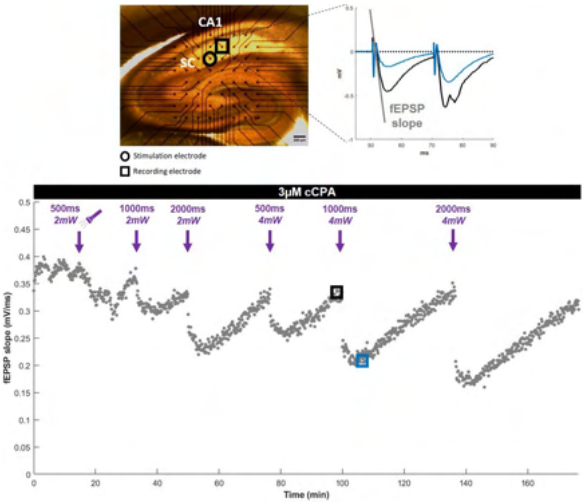
Background and aims: Adenosine A1 receptors are capable of modulating neuronal activity by pre- and postsynaptic routes, offering promising possibilities for therapeutic intervention. Unfortunately, their use is limited by the ubiquity of A1 receptors, highlighting the need for focal activation. Optopharmacology allows site-specific agonist release and receptor activation using light-sensitive caged compounds. Here we investigated the UV-triggered activation of the coumarin-caged A1 agonist N6-cyclopentyladenosine (cCPA) in the CA1 region of acute rat hippocampal slices.

Methods: CA1 field potentials (fEPSPs and population spikes(PS)) were evoked by electrical stimulation of the Schaffer collaterals with variable intensity and recorded using 60-channel multielectrode arrays. Superfusion with 3µM cCPA and UV-pulses (LED: 405nm) at two power intensities (2 and 4mW) for 500 (n=3), 1,000 (n=5) and 2,000ms (n=5) duration induced transient releases of CPA that modulated synaptic transmission and neuronal excitability as quantified in the local field potentials.

Results: They reduced fEPSP slopes for both power intensities and three durations to respectively 81±2%, 55±7% and 40±5% of baseline value. The effects are reversible as demonstrated by the stable and repeated modulation of A1 signalling within the same slice. A similar effect but of larger magnitude was observed for the PS. A computational model allowed us to interpret the observed temporal transients in neuronal excitability and enabled the generation of illumination strategies.



Conclusion: These data provide 1st proof that UV-triggered uncaging of cCPA can be used for controlled transient inhibition of excitatory transmission in slices, making optopharmacology a promising tool for focal modulation of neuronal activity in disease models like epilepsy.

Disclosure: This work was supported by grants from Research Foundation – Flanders (FWO; 1216520N & 1S65521N) and the Queen Elisabeth Medical Foundation (GSKE) for Neurosciences.

EPR-025

Abstract withdrawn

EPR-026

Intracellular zinc may mediate the pro- or anti-seizure effects exerted by GPR39-zinc receptor agonist

U. Doboszewska [1], J. Sawicki [2], M. Pierog [1], K. Socala [1], D. Nieoczym [1], B. Szewczyk [3], A. Rafalo-Ulinska [3], M. Mackowiak [3], I. Sowa [2], P. Wlaz [1]
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Background and aims: The G-protein coupled receptor 39 (GPR39) is activated by zinc ions and has been suggested as a novel drug target for epilepsy. However, TC-G 1008, a potent and selective GPR39 agonist, exerted either seizure-threshold-decreasing or -increasing effects, in the maximal electroshock seizure (MES)-threshold (MEST) test and the 6-Hz-threshold test, respectively. In an attempt to find mechanisms that may underlie these distinct effects, we measured total and intracellular zinc ([Zn2+]i) concentrations.
Methods: Male Albino Swiss mice were injected i.p. with a single dose of TC-G 1008 (2.5, 20 or 40 mg/kg) or ZnCl2 (4, 8 or 16mg Zn/kg). 30 min later the mice were stimulated with supramaximal MES stimulus of 50 mA or supramaximal current intensity of 32 mA. Serum zinc concentration was measured using Inductively Coupled Plasma Optical Emission Spectrometry. [Zn2+]i was measured in hippocampal sections using membrane-permeable fluorescent probe Zinpyr-1. Data were analyzed using Image J and Graph Pad Prism v. 5.03, by the 2-way ANOVA followed by a Bonferroni post hoc test.
Results: The changes in serum zinc were not parallel to changes in hippocampal [Zn2+]i. Administration of the noneffective in the MEST test dose of TC-G 1008 as well as administration of seizure-threshold increasing in the 6-Hz test doses of TC-G 1008 or ZnCl2 and an electrical stimulus were associated with decreased [Zn2+]i in the CA1, CA3 and DG regions of the hippocampus vs. vehicle-treated mice that received an electrical stimulus.
Conclusion: Decreasing [Zn2+]i in the hippocampus may be a strategy for reducing seizures.
Disclosure: The study was supported by a grant from the National Science Centre, Poland (2016/20/S/NZ7/00424).

EPR-027

Safety and Tolerability Profile of Antiseizure Medication in the Elderly

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Background and aims: Epilepsy is particularly common in the elderly however, most clinical trials ignore this age group. The high percentage of co-morbidities, polymedication, and age-related pharmacokinetic changes subject these patients to an increase in the severity and number of side effects (SE) of antiseizure medication (ASM).
Methods: Data were retrospectively collected from elderly epileptic outpatients (over 65 years old) at a Hospital centre from January 2018 to August 2020. The categorical variables were compared using the chi-square test. Continuous variables were evaluated using t-tests for independent samples or non-parametric tests, depending on the normality of the distribution.
Results: Data were collected from 77 patients, 43 women, and 34 men, mean age of 75.14 years. 49.4% of these patients had one or more SE. The most common SE were cognitive symptoms (8.2%), depression (7.3%), and irritability (6.7%). The appearance of SE was positively correlated with the age group of 75 years or older (p=0.03). The use of Levetiracetam was inversely correlated with the appearance of SE (p=0.05), in contrast to what happened with Phenytoin (p=0.019) and Eslicarbazepine (p=0.041).
Conclusion: The ASM's SE were extremely frequent, appearing in almost 50% of the sample, increasing in frequency with age. The safety profile obtained favours the use of Levetiracetam and disfavour the use of Eslicarbazepine and Phenytoin. Although the study is retrospective, without taking into account the doses of ASM, the results highlight the importance of conscientious use and careful selection of ASM in the elderly.
Disclosure: The authors declare that they have no conflict of interest.

Headache and Pain 1

EPR-028

Altered connectivity in sensorimotor-insular regions during spontaneous migraine attacks: a resting-state study.

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Background and aims: Migraine is one of the most prevalent disorders globally and the first cause of disability in women worldwide. It manifests through episodic attacks of a throbbing head pain, accompanied by autonomic, sensory, affective and cognitive dysfunction. Evidence of neuronal changes in migraine has been provided by fMRI studies. In particular, functional connectivity (FC) alterations were found in several resting state networks (RSNs) when comparing different phases of the migraine cycle.
Methods: This investigation consists on the prospective longitudinal study of 11 women with episodic migraine without aura evaluated through resting-state fMRI (rs-fMRI) during a spontaneous attack and in the interictal phase. An exploratory independent component analysis (ICA) was applied to rs-fMRI data to derive RSNs and, for each RSN, differences in within-network mean FC between the ictal and interictal states were assessed. A post-hoc analysis evaluated the relations between RSNs' FC and clinical features.
Results: 21 RSNs were extracted and significant within-network FC differences were found between the ictal and interictal states in a sensorimotor-insular network, including regions of the primary somatosensory cortex, primary motor cortex and the posterior insula. Individuals with usual longer attacks showed lower FC in this RSN, for both ictal and interictal sessions.
Conclusion: To our knowledge, we present the 1st study of FC in spontaneous migraine attacks revealing differences between migraine-states in the sensorimotor-insular network, associated with pain processing and perception, with relevant roles in pain intensity and spatial discrimination pathways.
Disclosure: This investigation has not been granted with any commercial or institutional support.

EPR-030

A new MRI radiological sign in HaNDL syndrome: description of two cases

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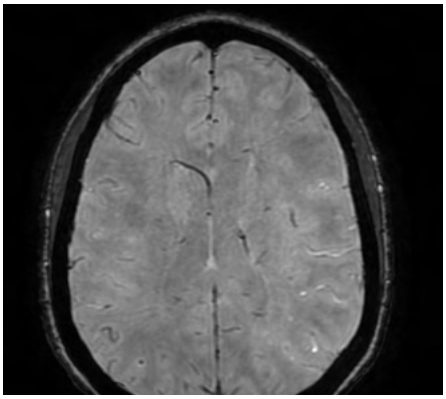
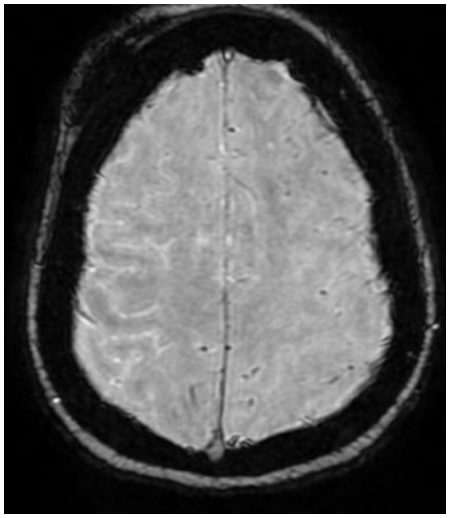
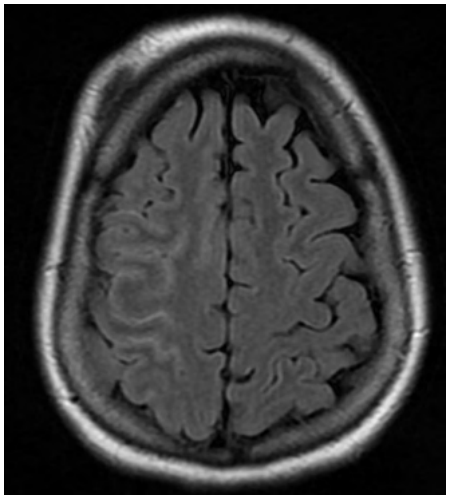
Background and aims: Syndrome of transient Headache and Neurological Deficits with cerebrospinal fluid Lymphocytosis (HaNDL) is usually a diagnostic challenge due to the absence of a biomarker that makes easier the differential diagnosis with severe neurological diseases such as encephalitis or stroke. Magnetic Resonance Imaging (MRI) is often described as normal, however, some reversible alterations have been recently being described.
Methods: We report two cases that fulfill criteria of HaNDL syndrome. We describe the clinical presentation and neuroimaging.
Results: The 1st case is a woman of 35 years old, with three episodes of right hemiparesis, motor aphasia and intense headache. Lumbar puncture revealed lymphocytic pleocytosis with hyperproteinorrhaquia. CT was normal. The second case is a woman of 36 years old, with Crohn disease treated with adalimumab, who after two weeks of headache developed right hemiparesis and dysarthria. CT showed right parietal swelling and angioTC revealed narrowed right middle cerebral artery. CSF had lymphocytic pleocytosis without hyperproteinorrhaquia Both patients showed MR susceptibility weighted sequences (SWI) with a reduced venous signal in the symptomatic hemisphere.



SWI RMI PATIENT 1: Left hemisphere with reduced venous signal in SWI



SWI RMI PATIENT 2: Right hemisphere with reduced venous signal in SWI



FLAIR MRI PATIENT 2: Left parietal swelling

Conclusion: The reduced venous signal within the symptomatic region seen in MRI-SWI was recently reported in one case of HaNDL syndrome. This is possibly caused by the decreased oxygen extraction fraction, that could indicate a decrease in metabolic demands or a fail in oxygen employment by the affected tissue. We report two additional cases with this sign, that could represent an useful clinical tool in the diagnosis.
Disclosure: Nothing to disclose

EPR-031

Extreme ecchymoses in a migraine patient using concomitant treatment with erenumab and fish oil supplements

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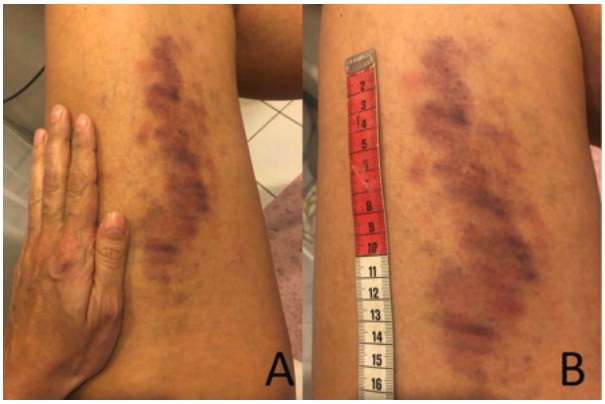
Background and aims: Erenumab, a monoclonal antibody against the calcitonin gene-related peptide (CGRP) receptor, is registered for migraine prevention. Compared to other conventional migraine prevention medicines erenumab has better tolerability. Impaired hemostasis has not been reported previously. Here, we report the first case of an increased tendency to bruises in a migraine patient treated with erenumab.
Methods: Case report
Results: A 41-years old female migraine patient was treated with erenumab for 12 months, which led to a significant reduction of headache and migraine days. three months after treatment start, she experienced increased tendency to bruises leading to extreme ecchymosis after four months treatment. Platelet counts and aggregation, thrombo-elastography, activated partial thromboplastin time (APTT) and international normalized ratio (INR) were all normal. Thorough, interview revealed intake of fish oil supplements for many years prior to treatment. The increased tendency to bruises subsided after discontinuation of fish oil supplements.



Ecchymoses on the patient's upper left thigh with (A) patient's hand for scale, and B) with a ruler.

Conclusion: The combination of fish oil supplements and erenumab may cause increased tendency to bruises. Erenumab has no effect on the platelets per se but may cause impaired wound healing by suppression of CGRP. Thus, small and unnoticeable bruises may aggravate instead in patients with tendency to bruises caused by for instance fish oil supplements.
Disclosure: MA: AbbVie, Allergan, Amgen, Eli Lilly, Lundbeck, Novartis, and Teva. FMA: Eli Lilly, Novartis, Teva, Lundbeck.

EPR-032

Intravenous sodium valproate for acute migraine: a meta-analysis

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Background and aims: Oral sodium valproate is being widely used and approved by Food and Drug Administration (FDA) in treatment of acute migraine, but in recent years intravenous sodium valproate (iVPA) has been shown to be safe and effective for patients with acute migraine attack. However, published studies show heterogeneous results of iVPA effectiveness. The aim of our study was to evaluate the efficiency and safety of iVPA in patients with acute migraine.

Methods: Two researchers independently searched the PubMed and Cochrane Library databases for randomized controlled trials (RCT) that investigated the efficiency of iVPA in acute migraine. The entire texts of included publications were overviewed and data was collected. The primary outcome was improvement of headache intensity and headache relief. Recurrence of headache and number of adverse events was also analysed.

Results: Four trials involving 203 patients were included in the review. Our meta-analysis showed that patients receiving iVPA had similar improvement of headache intensity and rate of headache relief (OR: 1.19, 95% CI: 0.40 to 3.43, p=0.75) to patients receiving other active comparators. Subgroup analysis showed that iVPA was superior to metoclopramide in the individual study.

Study	Country	Design	Patients	Mean age (years)	Treatments	
					iVPA	Control
Bakhshayesh B., 2013	Iran	Prospective open-label RCT; Parallel	Acute migraine without aura, lasting for =<24h	31.52	VPA 400 mg diluted into 100 mL D5W intravenous	Metoclopramide 10 mg intramuscular followed by sumatriptan 6 mg subcutaneous
Edwards K.R., 2001	USA	Open-label RCY; Parallel	Acute migraine with or without aura, lasting for =<96 h	42	VPA 500 mg diluted into 100 mL D5W	Metoclopramide 10 mg intramuscular followed by dihydroergotiamine 1 mg intramuscular
Karimi N., 2017	Iran	Double-blinded RCT; Parallel	Acute migraine without aura, lasting for <6 d	33.64	VPA 400 mg diluted into 4 mL normal saline intravenous	Dexamethasone 8 mg diluted into 4 mL normal saline intravenous
Foroughipour M., 2013	Iran	Double-blinded RCT; Parallel	Acute migraine, lasting for >72 h	33.36	VPA 900 mg diluted in 150 mL normal saline intravenous drip over 10 min	Dexamethasone 16 mg diluted in 150 mL normal saline intravenous drip over 10 min

Table 1. Demographic and clinical characteristics of included studies

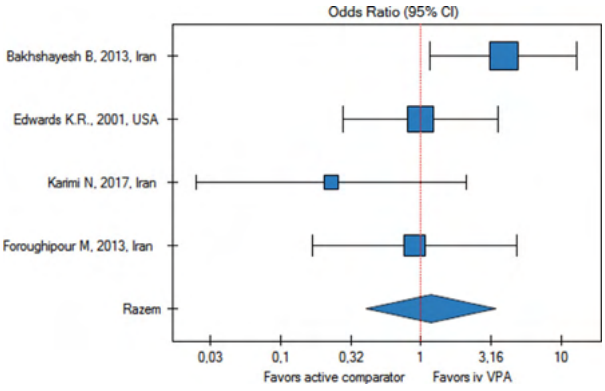

Figure 1. Forest plot of iVPA vs other active comparators for improvement of headache intensity

Conclusion: iVPA was comparable to the studied comparators for aborting migraine attack. Although we did not observe superiority of VPA over comparators in the meta-analysis, it can be a reasonable alternative for the treatment of migraine attacks in the emergency, especially for patients which, for any reason, cannot take other medicines. More studies on the effectiveness of iVPA in acute migraine are needed.

Disclosure: No conflict of interest.

EPR-033

Structure and frequency of headache in patients with dolichoarteriopathies of the internal carotid arteries

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Background and aims: The complaints of patients with dolichoarteriopathies of the internal carotid artery (DICAs) are characterized by clinical diversity, and the most frequent of them are headache, dizziness, visual impairments and increased fatigue. In this regard, it is relevant to study the prevalence of different headache types in responders with DICAs. The goal of our study was to analyze the frequency and structure of headaches in patients with DICAs.
Methods: The prospective study included 98 patients with DICAs in age from 26 to 51 years. The diagnosis of headache met International Classification of Headache Disorders, 3rd edition (ICHD-3) criteria. The data were analyzed with MS Excel software.
Results: The gender composition of the studied respondents included 70 women (71,4%) and 28 men (28,6%), with an average age of 42,5±8,1 years. Among all patients with DICAs, 56 people (57,2%) complained of headaches. The majority of the studied patients (91,1%) had primary forms of headache: tension-type headache (TTH) was diagnosed in 43 people (76,8%), migraine – in eight patients (14,3%). The secondary headache in the form of cervicogenic headache was diagnosed in 5 (8,9%) patients.

Different headaches in patients with dolichoarteriopathies of ICA, n=56

Primary headaches				Secondary headache	
Migraine		Tension-type headache (TTH)		Type	Amount
Type	Amount	Type	Amount	Cervicogenic headache	5
Migraine without aura	5	Ihfrequent episodic TTH	30		
Migraine with aura	3	Frequent episodic TTH	11		
Chronic migraine	0	Chronic TTH	2		
Total	8	Total	43	Total	5

Different headaches in patients with dolichoarteriopathies of internal carotid arteries (ICA)

Conclusion: Headaches are widely presented in patients with dolichoarteriopathies of the internal carotid arteries. At the same time, the majority of patients had primary headaches and only 8,9% of patients in our study suffered from a secondary headache,
Disclosure: Nothing to disclose.

EPR-034

Eptinezumab Treatment Initiated During a Migraine Attack Prolonged the Time to Next Migraine and Improved HIT-6 Outcomes

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Background and aims: Eptinezumab, a humanized anticalcitonin gene-related peptide monoclonal antibody, is an approved treatment for migraine prevention. These RELIEF analyses evaluate the effect of eptinezumab on time to next migraine and the 6-item Headache Impact Test (HIT-6) when administered during a migraine in patients considered candidates for preventive therapy.
Methods: RELIEF was a parallel-group, double-blind, placebo-controlled study (NCT04152083). Eligible patients (aged 18–75y with migraine on 4–15d/mo in 3mo prior to screening) were randomized to infusion with eptinezumab 100mg (n=238) or placebo (n=242) within 1–6h of qualifying migraine start. The RELIEF study met all primary and secondary efficacy endpoints which are presented separately. Exploratory endpoints reported herein included time to next migraine (from Day 3 to start of next patient-reported migraine) and change from baseline to Week four in HIT-6 total score.
Results: Median time to next migraine was 10 days in the eptinezumab group and five days in the placebo group (hazard ratio=0.60; $p<0.0001$). Mean HIT-6 total scores at screening visit indicated severe life impact (eptinezumab, 65.1; placebo, 64.8). At four weeks post-infusion, eptinezumab demonstrated clinically meaningful improvement in HIT-6 total score compared with placebo (mean change from baseline: eptinezumab, -8.7; placebo, -4.5; mean [95%CI] difference from placebo: -4.2 [-5.75, -2.63], $p<0.0001$).
Conclusion: In candidates for preventive migraine therapy, results from RELIEF showed that the preventive treatment eptinezumab delayed time to next migraine vs placebo even when initiated during a migraine attack. HIT-6 results demonstrated clinically meaningful reductions in patient-reported and migraine-related impact over four weeks following eptinezumab versus placebo infusion.
Disclosure: H. Lundbeck A/S, Copenhagen, Denmark

EPR-035

HEMIPLEGIC MIGRAINE, DYNAMIC MRI FINDINGS AND MIGRAINOUS INFARCTION

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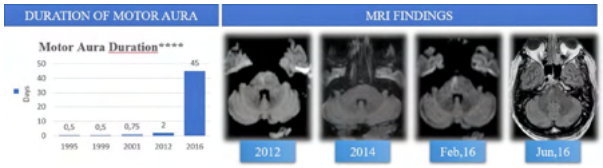
Background and aims: Hemiplegic migraine (HM) is a rare variant of migraine in which symptoms of motor weakness occur during the aura. Migrainous infarction (MI) is a migraine complication, that occurs very rarely in patients with HM. During attacks of HM, brain imaging is usually normal although cortical edema, transient prominence of the cerebral veins and restricted, normal or increased diffusion on DWI sequences were reported, in single cases
Methods: Case-report
Results: We report the case of a male patient whose HM symptoms started in his twenties but, over the years, experienced increasingly prolonged periods of motor weakness. MRI performed during one of his long-lasting attacks showed reversible abnormally low ADC values in the same area. Then, years later, he developed a migrainous infarction.



brain_MRI

Conclusion: To our knowledge, this is the 1st report of an HM patient in whom his auras increased in clinical complexity over the years 1st related to dynamic MRI abnormalities and later to MI. In this report, we discuss the origin of the motor aura as well as the association between the duration of aura and the likelihood of brain ischemia
Disclosure: No disclosures.

Miscellaneous: Child neurology, Infectious diseases, Neuro-oncology

EPR-036

NODDI disclose early changes in the normal appearing white matter in pediatric onset multiple sclerosis.

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Background and aims: Pediatric-onset multiple sclerosis (POMS) is characterized by high degree brain inflammation and rapid accumulation of white and grey matter damage.
Methods: Abnormalities in the normal appearing white matter (NAWM) and their clinical relevance in POMS were investigated by Neurite Orientation Dispersion and Density Imaging (NODDI). Eighteen POMS and 10 age- and sex-matched healthy controls (HCs) underwent a 3T brain MRI; clinical disability was assessed through the Expanded Disability Status Scale (EDSS). Individual maps of orientation dispersion index (ODI) and neurite density index (NDI) were obtained. Between-group differences in diffusion tensor/NODDI measures were investigated in the corpus callosum (CC), cortico-spinal tract (CST) and posterior thalamic radiation (PTR). Their association with clinical scores were also evaluated.
Results: Compared to HCs, POMS had lower NDI values in the NAWM of all the investigated tracts (p0.041). PTR showed also lower FA (p=0.008) and higher MD (p=0.040) values. CC FA was inversely associated with EDSS (r=-0.707, p=0.001), whereas CC MD and ODI were directly associated with EDSS (r=0.580, p=0.012; r=0.574, p=0.013). In the PTR, EDSS correlated with FA (r=-0.625, p= 0.006) and ODI (r=0.592, p=0.010). In the CC, lower FA associated with a higher lesion load within tract (r=-0.588, p=0.010), whereas higher MD associated with lower lesion load within tract (r=0.663, p=0.003). Similarly, PTR lesion load correlated with FA (r=-0.642, p=0.004) and ODI (r=0.592, p=0.010) within tract.
Conclusion: A reduced neurite density was observed in the NAWM of POMS, providing further insights on the mechanisms underpinning neurodegeneration in this peculiar population.
Disclosure: Nothing to disclose.

EPR-037

A stratified approach to identifying and investigating neonatal seizures: a service evaluation

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Background and aims: Diagnosing and managing neonatal seizures can be challenging. This service evaluation assessed current diagnostic investigations used at a regional neonatal intensive care unit from 2016–2020.
Methods: Electronic medical records of all neonates with suspected seizures at the Rosie Hospital, Cambridge, UK from February 2016 to August 2020 were retrospectively reviewed. 135 patients were identified, and data on their presentation, investigations and management evaluated.
Results: Of the 135 neonates, 85 (63%) had electroclinical, 38 (28%) clinically-suspected only, and 12 (9%) electrical-only seizures. 130 infants (96%) had amplitude-integrated electroencephalogram monitoring (aEEG), with seizures detected in 97 (75%). 124 (92%) had EEG, with seizures recorded in 39 (31%). 116 (86%) neonates had a cause of their seizures diagnosed, most frequently hypoxic-ischaemic encephalopathy (HIE) (64%). Magnetic resonance imaging (MRI) commonly found evidence of HIE (33%) and intracranial haemorrhage (17%). Genomic microarray analysis in 34 infants found three cases of clinical significance (9%). Whole genome sequence (WGS) analysis in 37 infants identified pathogenic variants in five infants (14%), including three monogenic mutations known to cause early epileptic encephalopathy, enabling early tailored antiepileptic therapy.

Table 1: Clinical characteristics and seizure aetiology among 135 neonates with clinically-suspected, electrical or electroclinical seizures

	Overall N = 135
Clinical Characteristics	
Male	79 (59%)
Term (≥37 weeks gestation)	105 (78%)
Resuscitation needed at birth	113 (84%)
APGAR <7 at 10 mins	48 (36%)
Seizure type	
Electrical only	12 (9%)
Clinically-suspected only	38 (28%)
Electroclinical	85 (63%)
aEEG	
aEEG performed	130 (96%)
Seizures identified	97 (72%)
EEG	
EEG performed	124 (92%)
Seizures identified	39 (29%)
Seizure Aetiology	
HIE	86 (64%)
Intraventricular/parenchymal haemorrhage	11 (8%)
Neonatal stroke	7 (5%)
Sepsis/congenital infection	3 (2%)
Skull fracture and intracranial haemorrhage	2 (1%)
Hypoglycaemia associated brain injury	1 (1%)
Other	5 (4%)
Unknown	20 (15%)

Clinical characteristics and seizure aetiology among 135 neonates with clinically-suspected, electrical or electroclinical seizures

Conclusion: Similar to other studies, many infants (28%) with clinically-suspected seizures had no aEEG correlate, suggesting abnormal movements were mistakenly diagnosed as seizures. This reinforces the importance of electrophysiological assessment, ideally with full video-EEG. Key factors yielding diagnosis were clinical scenario evaluation and MRI. Genetic testing identified an important patient group with genetic diagnoses. Continuous video-EEG alongside stratified investigations could enable more accurate seizure detection and earlier diagnosis of rare conditions, with important management implications.

Disclosure: This research has not been granted any commercial or institutional support.

EPR-038

Diffusion Kurtosis Imaging of microstructural alterations in the brains of infants with hypoxic-ischemic encephalopathy

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Background and aims: Our aim was to assess microstructural alterations in the cerebrums of infants with hypoxic-ischemic encephalopathy (HIE) using diffusion kurtosis imaging (DKI).

Methods: 31 neonatal patients with HIE and 18 age-matched healthy volunteers were examined via DKI using a 3.0T MRI. DKI values were computed for 32 cerebral regions in both the controls and the HIE patients. The infants with HIE in DKI group were divided into three groups according to the clinical grading, DKI parameters was evaluated for detection of different groups in HIE infants, sensitivity, specificity and area under the SROC curve.

Results: 1. Compared to the control group, MK and KR of posterior limb of internal capsule, MK of splenium of corpus callosum, KA of cingulate gyrus, MK and KR of parietal lobe were all decreased in the HIE group. 2. ROC of DKI parameters in mild group and moderate group or severe group were analyzed. Posterior limb MK of internal capsule in the differential diagnosis of moderate and severe group demonstrated the highest diagnostic performance, with an AUC of 0.994. The sensitivity and specificity were 100% and 88.89%, respectively. The best threshold was 0.8889. Compared with the good prognosis group, KR of posterior limb of internal capsule in the poor prognosis group decreased significantly.

Conclusion: DKI offers comprehensive measurements for quantitative evaluation of microstructural changes in both white and grey matter in HIE patients. DKI scans of infants with HIE exhibiting significant decreases in MK and KR might play an important role in evaluating the severity of HIE.

Disclosure: This study were Grant for Key Disciplinary Project of Clinical Medicine under the Guangdong High-level University Development Program, China and Clinical teaching reform project in Guangdong Province China 2018 JD058

EPR-039

Meningitis In Brazil: Comparative Overview Between Incidence And Vaccination Coverage In The Last Decade

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Background and aims: According to World Health Organization, there was almost one million suspected cases of meningitis in the world in the past 20 years. In Brazil, the main form of prevention has been vaccination against Haemophilus influenzae type B, meningococcus and pneumococcus. Thus, it is relevant to analyze vaccination coverage (VC) and the incidence of meningitis in Brazil from 2010 to 2020.
Methods: Epidemiological, retrospective, observational study, accomplished through the Hospital Information System of Brazilian Unified Health System (SIH/SUS/DATASUS), from 2010 until 2020.
Results: In last decade, in Brazil, 187,508 cases of meningitis were registered. When analyzing year by year, there was a high contrast between the number of cases from 2010 (n=20,536) to 2020 (n=4,411), representing a 78.5% reduction in the incidence of meningitis. There was also a significant decrease in cases per 100,000 habitants, from 10.7 cases/100,000 habitants in 2010 to 2.3 cases/100,000 habitants in 2020. When analyzing VC, there were lower rates of vaccination in Brazilian population in 2010 (50.9%) compared to subsequent years, especially in 2011, 2013 and 2015, which reached the highest VC (95.4%; 95.4%; 92.8%, respectively).

Year	Vaccination Coverage	Incidence
2010	50,92	10,7
2011	95,44	10,9
2012	84,5	11,4
2013	95,37	10,1
2014	92,36	9,2
2015	92,82	8,4
2016	74,24	8,2
2017	83,62	8,9
2018	86,49	9,2
2019	86,43	8,3
2020	73,82	2,3

Conclusion: There was an exponential reduction in the incidence of meningitis in Brazil, between 2010 and 2020, simultaneously with the increase in VC. The data obtained suggests that efforts to maintain high vaccination rates can contribute to eradication of this disease in Brazil.
Disclosure: There are no conflicts of interest.

EPR-040

The coronavirus pandemic and its repercussions on hospitalization for meningococcal infection in Brazil in 2020

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Background and aims: Meningococcal infection is transmitted mainly through respiratory secretions and saliva. For that, it is important to assess the impacts of the COVID-19 pandemic, through measures of social isolation and mandatory use of masks, on the meningococcal transmission chain.
Methods: The first semesters of the years 2016 to 2019 and 2020 were compared. Data on hospitalizations were extracted from the Hospital Information System (SIH). Variables analyzed: absolute number of hospitalizations and percentage of hospitalized patients by age group.
Results: Regarding the number of hospitalizations, the average in the period from 2016 to 2019 was 529.25; in 2020, 278. About hospitalizations by age group ("average of 2016–2019", "average of 2020"): children under one year old (13.31%, 13.79%); from 1–19 years (27.7%, 40.62%); from 20–59 years (39.57%, 33.77%); individuals over 60 years (19.42%, 11.81%).
Conclusion: In 2020, there was a 45.88% reduction compared to the previous four years. Thus, social isolation, increased individual health measures probably caused a decrease in meningococcal transmission. The absence of teaching activities justifies the 13% reduction in hospitalizations between 1–19 years. In the group from 20 to 59, it increased by 6%, probably by being active at work and therefore more exposed. In the elderly, hospitalizations increased 8%, possibly because they probably had work activities. Thus, individuals aged 20–59 or more started to represent a higher percentage among hospitalized patients, despite the reduction in the total number of hospitalizations.
Disclosure: Nothing to disclose.

EPR-041

Spectrum of CNS infections in a Tertiary Health Care Centre in Cameroon

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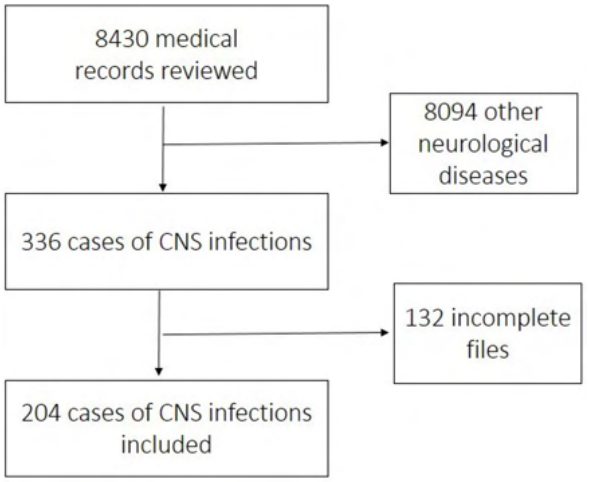
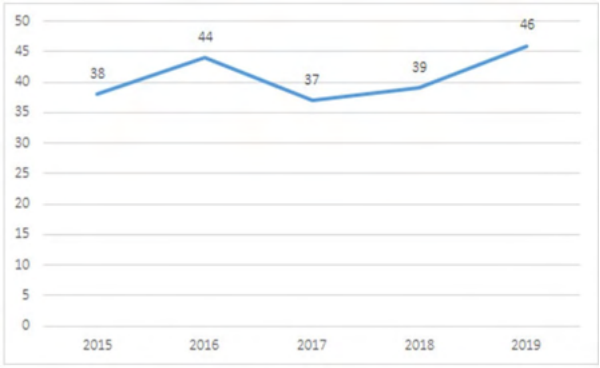
Background and aims: Central nervous system (CNS) infections are serious and debilitating diseases with significant mortality, and high prevalence in the context of HIV pandemic in Africa. We aimed to determine the epidemiological, clinical and outcome of CNS infections at the Douala General Hospital (DGH), Cameroon.
Methods: To carry out this study, we collected the medical records of patients hospitalized for CNS infections in the internal medicine department of DGH from January 2015 to December 2019. Only the records of patients diagnosed on the basis of neuroimaging (CT scan or MRI) and/or biological (CSF) were retained in this study. SPSS 23.0 software was used for data entry and analysis.

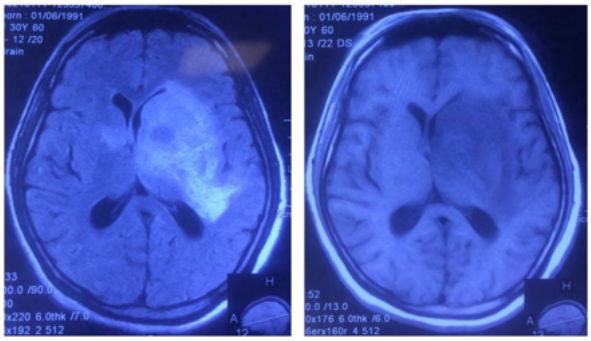


Flow chart of patients' inclusion

Results: Among the 204 patients included in the study, 54.4% were male. 147 patients were HIV positive, with 38.1% of them (n=56) on regular followed up. The most common clinical signs were fever (84.8%) and headache (68.6%). The main aetiologies were: cerebral toxoplasmosis (24.5%), cryptococcal meningitis (21.1%). Tuberculous meningitis was found in six patients (2.9%). Of the 143 CSF samples collected, 70.6% (n=101) were sterile. Unknown cause was independently associated to in-hospital mortality (22.1%).



Progression of CNS infections from 2015 to 2019



Left basal ganglia cerebral toxoplasmosis on Brain MRI

Conclusion: CNS infections are frequent, with HIV as the main comorbidity. Fever and headache are the commonest signs. The main causes are HIV related opportunistic infection. More than one patient in five die during hospitalization.
Disclosure: Nothing to disclose.

EPR-042

Distinguishing Pseudoprogression from true Progression in Glioblastoma using MRI Tumor Microenvironment (TME) Imaging.

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Background and aims: Distinguishing Pseudoprogression from true Progression in patients with Glioblastoma after receiving standard concomitant radiochemotherapy can be challenging. The incidence of Pseudoprogression after radiochemotherapy varies within studies from 10–30%.
Methods: Pseudoprogression and true Progression were diagnosed according to histological and/or radiological criteria. A novel MRI approach for noninvasive visualization of the tumor microenvironment (TME) was established in order to gain information concerning oxygen metabolism and neovascularization. Five different TME compartments were classified including necrosis, hypoxia with/without neovascularization, oxidative phosphorylation, and glycolysis. Patients were identified and analyzed retrospectively from the institutional brain tumor databank.
Results: 12 Patients with histological (n=4) or imaging (n=8) confirmed Pseudoprogression, and 23 Patients with histological (n=17) or imaging (n=5) confirmed true progression were included in this pilot study. Patients with Pseudoprogression showed different patterns with respect to oxygen metabolism and neovascularization as compared to patients with true progression. Patients with pseudoprogression showed significant higher percentage of tumor volume for necrosis ($p<0.001$; 49.7% necrosis in PsP patients vs. 23.9% necrosis in true progression patients) and hypoxia ($p<0.002$; 26.2% vs. 10.8%) as well as significant lower percentage of tumor volume with neovascularisation ($p<0.001$; 24.0% vs. 65.3%) and active tumor ($p<0.001$; 9.4% vs. 48.3%), respectively.
Conclusion: The phenomenon of Pseudoprogression is still puzzeling and a clinically relevant problem. False diagnosis of Progression or Pseudoprogression may lead to inadequate treatment decisions. The implementation of MRI TME imaging, might increase the noninvasive discriminatory power for true Progression and Pseudoprogression.
Disclosure: Nothing to disclose.

EPR-043

Prognostic characteristics in adult brainstem glioma: a case series from two Austrian brain tumour centres

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Background and aims: Adult brainstem gliomas (BSGs) are rare central nervous system tumours and characterized by a highly heterogenous clinical course. Median survival times range from 11 up to 84 months. Therapy is restricted to radio- and chemotherapy although no standardized international treatment guidelines exist yet. We investigated clinical and radiological data to assess prognostic features providing support for treatment decisions.
Methods: 34 BSG patients treated between 2000 and 2019 and aged 18 years at diagnosis were retrospectively identified from the databases of the two largest Austrian Neuro-Oncology centres. Clinical data including baseline characteristics, clinical disease course, applied therapies, outcome and neuroradiological findings were gathered and analysed. The tumour median apparent diffusion coefficient (ADC), volumetry of contrast-enhancing and non-contrast-enhancing lesions were determined on magnetic resonance imaging scans performed at diagnosis.
Results: Patients' characteristics are outlined in Table 1. Tumour progression occurred in 26/34 (76.5%) patients after a median follow up time of 19 months (range 0.9–236.2). Median overall survival (OS) and progression free survival (PFS) was 24.1 months (range 0.9–236.2; 95% CI 18.1–30.1) and 14.5 months (range 0.7–178.5; 95% CI 5.1–23.9), respectively. Low performance status, high body mass index (BMI) at diagnosis and WHO grading were associated with shorter PFS and OS at univariate analysis ($p<0.05$, log rank test, respectively). ADC values below the median were significantly associated with shorter OS (14.9 vs 44.2 months, $p=0.018$).

Table 1: Patients' characteristics

	n=34	%
Gender		
male	18	52.9
female	16	47.1
Median age at diagnosis, years (range)	38.5 (18-71)	
Median BMI at diagnosis, kg/m² (range)	25.6 (17.4-38.1)	
Clinical presentation at diagnosis		
< 2 symptoms	4	11.8
2 or more symptoms	30	88.2
Histological confirmation (biopsy performed)		
yes	27	79.4
no	7	20.6
Histopathological diagnosis n=27		
WHO II	4	11.8
WHO III	14	41.2
WHO IV	9	26.5
Integrated Diagnosis (WHO 2016) n=27		
Diffuse astrocytoma		
IDH wildtype	2	7.4
IDH mutated	2	7.4
Anaplastic astrocytoma		
IDH wildtype	8	29.6
IDH mutated	2	7.4
Not otherwise specified	4	14.8
Glioblastoma		
IDH wildtype	1	3.7
IDH mutated	1	3.7
Not otherwise specified	4	14.8
Diffuse midline glioma (H3K27M-mut)	3	11.1
First-Line treatment		
Combined radio/chemotherapy	20	58.8
Chemotherapy alone	3	8.8
Radiotherapy alone	5	14.7
Wait and see	2	5.9
No therapy due to rapid disease progression	3	8.8

Table 1

Conclusion: ECOG, BMI, WHO grading and ADC values were associated with survival prognosis of BSG patients and should be included in prognostic assessment.
Disclosure: This study was funded by the Clinician Scientist Program (Johannes Kepler University Linz)

EPR-044

Status epilepticus on the eeg in in PRES in children with oncohematological diseases.

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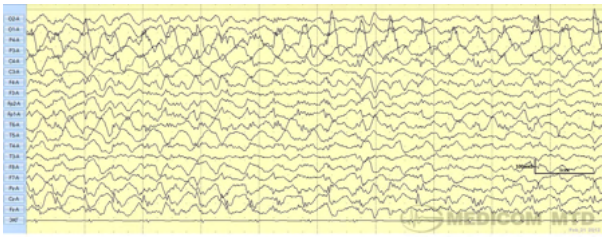
Background and aims: Posterior Reversible Encephalopathy Syndrome (PRES) is an acute, reversible condition, characterized by sudden onset with disturbance of consciousness, epileptic seizures, focal neurological symptoms. MRI shows changes in the white matter predominantly in the occipital-temporal-parietal areas. EEG changes in PRES are nonspecific (diffuse, regional, prolonged, periodic retardation) and epileptic activity. Patients with oncohematological diseases have a high risk of developing PRES, since they receive specific therapy.
Methods: A retrospective analysis of 20 electroencephalograms of children aged three to 15 years (male/female ratio =3:2) was carried out.
Results: A pattern of electrical status epilepticus was recorded on EEG in nine out of 20 children (45%) in the 1st 12 hours after the onset of PRES symptoms. Conducting an EEG as soon as possible after the development of the clinical picture of PRES reveals epileptiform activity, including electrical status epilepticus. This is important for the timely correction of therapy. The absence of seizures in the clinical picture and sedation does not exclude the registration of the EEG status epilepticus pattern; therefore, it is advisable to conduct an electroencelographic study in all patients with suspected PRES.



EEG of a patient with PRES, non-convulsive status epilepticus

Conclusion: Children with PRES diagnosed with MRI should have EEG monitoring within the first 12 hours from the manifestation of PRES.
Disclosure: PRES in children with hematologic cancer is often complicated by non-convulsive status epilepticus. Timely detection of status epilepticus allows to start AEDs and reduce the risk of epilepsy.

Movement disorders 1

EPR-045

Pharmacokinetic analysis of levodopa and carbidopa following subcutaneous infusion: A population pharmacokinetics model

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Background and aims: ND0612 is an investigational subcutaneous delivery system providing minimally invasive, continuous infusion of liquid levodopa/carbidopa under development for reliable, sustained relief of motor fluctuations in people with Parkinson's disease. We describe the population pharmacokinetics (PK) of levodopa and carbidopa following SC infusion with ND0612, with and without oral therapy, including associated interindividual variability and residual unexplained variability.
Methods: Two integrated population PK models (for levodopa and for carbidopa) were developed using data from Phase I studies of ND0612 in healthy volunteers (Study 004) and PD patients (Study 005). The predictive performance of the models was tested based on external Phase I data in healthy volunteers (Study 114). Model refinement was performed using aggregated data and will be continually updated as PK data from late-phase trials becomes available.
Results: Levodopa and carbidopa population PK were both adequately described by a one-compartment disposition model with 1st-order oral and SC absorption. Levodopa had parallel dopa decarboxylase (DDC) and COMT elimination from the central compartment, in which the inhibition of apparent DDC-mediated clearance was driven by carbidopa plasma concentrations. Carbidopa had linear elimination. Exploration of covariates revealed that age had a significant effect on apparent clearance and apparent volume of distribution for both carbidopa and levodopa, even after accounting for body weight differences; both parameters decreased with increasing age.
Conclusion: Model diagnostics for the carbidopa and levodopa population PK models indicated a satisfactory predictive performance, supporting their usability to derive individual predictions of exposure to be used in future pharmacokinetic-pharmacodynamic analyses.
Disclosure: Funded by NeuroDerm

EPR-046

Hereditary Spastic Paraplegias in Austria: The Innsbruck Cohort Study

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Background and aims: Hereditary spastic paraplegias (HSPs) are rare hereditary neurodegenerative diseases. Although heterogeneous, their clinical key features are spasticity and weakness of the lower extremities. Currently, more than 80 different HSP genes are known, presenting with variable phenotypes. Estimated prevalence rates of HSPs in Europe are 3–10/100.000. The aim of this study is to report on preliminary data of the first Austrian HSP-registry.
Methods: In the retrospective analysis, 98 HSP patients were included. 47 patients were recruited for the prospective registry. Standardized rating scales, including the Spastic Paraplegia Rating Scale (SPRS), were performed.
Results: Retrospective data was collected on 63 males (64.3%) and 35 females (35.7%). Diagnosis was genetically confirmed in 38.8%, variants of unknown significance (VUS) were found in 16.3% whereas 44.9% of HSP cases were not assigned genetically. SPG4 was the most prevalent form with 68.4%, followed by SPG11 and SPG21 in 7.9%. 47 patients, 32 (68.1%) of whom were male, were recruited for our prospective registry. Diagnosis was confirmed in 48.9%, VUS were found in 21.3% while no causative mutation was found in 29.8%. Again SPG4 was the predominant genotype with 69.6%, followed by SPG11 (13.0%) and SPG7 (8.7%). Mean age at onset was 34.1 (Standard deviation [SD] 16,9), mean SPRS score was 18.3 (SD 9.9).
Conclusion: This is the first report of an Austrian HSP cohort. Retrospective datasets of 98 patients were analysed, 47 of whom were recruited for the prospective registry. While SPG4 is the most common subtype in this cohort, rare forms like SPG21 appear in our sample.
Disclosure: This project is a cooperation with the treatHSP-network.

EPR-047

CSF neurofilament light chain for differentiating Parkinson's disease from atypical parkinsonian disorders: meta-analysis

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Background and aims: Atypical Parkinsonian disorders (APDs) consist of a range of rare neurodegenerative diseases that are often misdiagnosed as Parkinson's disease (PD).The aim of this study was to assess the efficacy of neurofilament light chain (NFL)-a marker of axonal damage-in the cerebrospinal fluid (CSF) to discriminate PD from APDs.
Methods: Based on PRISMA guidelines, MEDLINE database was systematically searched for peer-reviewed studies written in English published until 06/2020, reporting CSF NFL levels in patients with PD and APDs, including progressive supranuclear palsy (PSP), multiple system atrophy (MSA), corticobasal degeneration (CBD) and Lewy body dementia (DLB). Animal studies, reviews or studies written in non-English were excluded. Hedges' g standardized mean differences were calculated, and meta-analyzed with random-effects models. Hierarchical summary receiver operating characteristic (ROC) analyses were performed to evaluate diagnostic accuracy. Methodological quality of each study was assessed via QUADAS-2.
Results: From a total of 156 articles, 12 studies were finally included in our meta-analysis, involving 880 PD patients and 847 APDs patients. CSF NFL levels were 1.26 standard deviations higher in APDs in comparison to PD patients [g=1.26, 95% Confidence Intervals (CI):0.99–1.53). Regarding APD subgroups, compared to PD, CSF NFL levels were significantly higher in patients with PSP, MSA, CBD and DLB. Pooled areas under the curve (AUC) for differentiating PD from APDs were 0.941 (95%CI:0.916–0.965), corresponding to average sensitivities of 80% (95%CI:64–90%) and specificity of 87% (95%CI:81–91%).
Conclusion: These results support the high diagnostic accuracy of CSF NFL levels in differentiating PD from APDs, highlighting their usefulness as promising biomarkers.
Disclosure: Nothing to disclose.

EPR-048

Impact of advanced Parkinson's disease on caregivers: Evidence from five European countries

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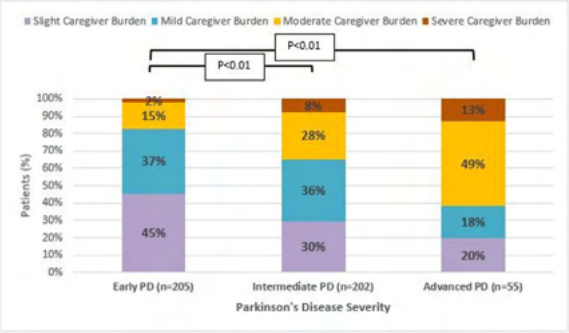
Background and aims: Parkinson's disease (PD) is a progressive neurodegenerative disorder leading to extensive burden impacting patients and caregivers. Recent studies identified the need for further understanding of the perceived burden and quality of life of Advanced PD (APD) caregivers.
Methods: Dyads of people with PD (PwP) and their primary caregivers were identified from a real-world data source (Adelphi DSP 2017-2019) across five European countries (UK, France, Italy, Spain, Germany). Incremental disease severity (early, intermediate, advanced) was assessed based on physician's judgement. Caregiver burden was assessed using Zarit Burden Index (ZBI), caregivers' health-related quality of life (EQ–5D), and medication intake due to caregiving. Incremental burden was evaluated using multivariable linear and logistic regression models (reference=early PD) adjusting for country, patient and caregiver demographic and clinical characteristics.
Results: The analytic sample (n=462 dyads) included 12% advanced, 44% intermediate, and 44% early PD. Caregivers (mean age= 62.7±12.7 years; 70.8% female) spent an average of 3.4±4.1 hours/week in PD-related caring activities. In advanced PD, the proportion of caregivers experiencing moderate-to-severe perceived burden (62%) was 3.6x higher than early PD ($p<0.01$) [Figure 1]. Adjusting for confounders, compared to early PD, caregivers of APD patients had significantly higher self-perceived burden (ZBI: +15.1, $p<0.01$), significantly worse quality of life (EQ-5D: -0.07, $p<0.01$) and were 5.3x more likely to start medications due to PD-related caregiving ($p<0.01$) [Table 1].



Notes: Caregiver perceived burden was measured using Zarit Burden Interview (ZBI) with categories interpreted as follows: Slight (Score 0-20), Mild (Score 21-40), Moderate (Score 41-60), and Severe (Score 61+).

Figure 1: Caregiver perceived burden by Parkinson's disease severity

Measure	Early PD (n=205)	Intermediate PD (n=202)	Advanced PD (n=55)
Caregiver Perceived Burden (ZBI Score)	23.5±16.9	32.7±17.3 [a]	39.9±18.4 [b,c]
Mean Difference (95% CI) [d]	Reference	8.5 (5.0, 11.9)	15.1 (9.7, 20.5)
Medications Intake due to Caregiving			
Yes	11.0%	26.9% [a]	38.9% [b]
OR (95% CI) [e]	Reference	2.5 (1.4, 4.4)	5.3 (2.4, 11.7)
Caregiver Quality of Life EQ-5D Score	0.93±0.13	0.87±0.16 [a]	0.85±0.25 [b]
Mean Difference (95% CI) [d]	Reference	-0.04 (-0.07, -0.01)	-0.07 (-0.12, -0.02)

Abbreviations: OR: Odds ratio; CI: Confidence Interval; ZBI: Zarit Burden Interview. **Notes:** a: statistically significant difference (p<0.01) between intermediate and early PD; b: statistically significant difference (p<0.01) between advanced and early PD; c: statistically significant difference (p<0.05) between advanced and intermediate PD; d: generalized linear model (gaussian, with identity link) adjusted for country, patient factors (age, sex, Charlson comorbidity index), and caregiver factors (age, sex, marital status); e: logistic regression model adjusted for country, patient factors (age, sex, Charlson comorbidity index), and caregiver factors (age, sex, marital status)

Table 1: Caregiver burden by Parkinson's disease severity

Conclusion: Caregivers of APD patients have incrementally higher perceived burden and worse health-related quality of life. Future studies should evaluate the impact of optimal PD symptom control on alleviating the burden of caregiving.
Disclosure: This study was supported by AbbVie, Inc. All authors contributed to the development of the abstract and maintained control over the final content.

EPR-049

Efficacy of opicapone according to levodopa's duration of use in Parkinson's disease patients with motor fluctuations

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Background and aims: Opicapone (OPC) proved to be effective in treating end-of-dose motor fluctuations (MF) in Parkinson's disease (PD) patients [1,2].
Methods: Matching OPC 50 mg and placebo (PLC) data from BIPARK-I and II [1, 2] were combined. The studies had similar designs, eligibility criteria and methodologies. Primary efficacy endpoint was change from baseline in absolute OFF-time. Safety was assessed by evaluating the incidence of treatment-emergent adverse events (TEAEs). Subgroup analyses were performed to evaluate consistency and potential trends between subgroups based on levodopa's duration of use at baseline (Table 1). Efficacy subgroup analyses were performed using Analysis of Covariance. Safety assessments were analysed descriptively.
Results: Overall, 522 patients were randomised to PLC (n=257) and OPC 50 mg (n=265) (Table 1). OPC 50 mg was significantly more effective than PLC for all subgroup analyses (p<0.05), except for the subgroup of patients treated with seven and eight years of levodopa use (Table 2). Moreover, OPC 50 mg demonstrated enhanced efficacy in patients who were lower in each subgroup threshold (Table 2). There was also a trend towards a lower incidence of dopaminergic-related TEAEs in the same subgroups of patients (Table 3).

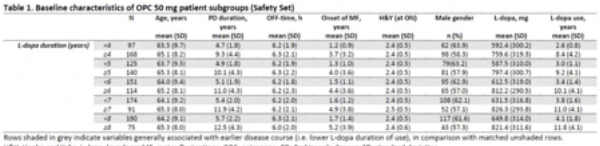

Table 1. Baseline characteristics of OPC 50 mg patient subgroups (Safety Set)

		N	Age, years mean (SD)	PD duration, years mean (SD)	OFF-time, h mean (SD)	Onset of MF, years mean (SD)	H&Y (at ON) mean (SD)	Male gender n (%)	L-dopa, mg mean (SD)	L-dopa use, years mean (SD)
L-dopa duration (years)	<4	97	63.5 (9.7)	4.7 (1.8)	6.2 (1.9)	1.2 (0.9)	2.4 (0.5)	62 (63.9)	592.4 (300.2)	2.6 (0.8)
	≥4	168	65.1 (8.2)	9.3 (4.4)	6.3 (2.1)	3.7 (3.2)	2.4 (0.5)	90 (56.3)	759.6 (319.3)	8.4 (4.2)
	<5	125	63.7 (9.5)	4.9 (1.8)	6.2 (1.9)	1.3 (1.0)	2.4 (0.5)	79(63.2)	567.5 (310.0)	3.0 (1.1)
	≥5	140	65.3 (8.1)	10.1 (4.3)	6.3 (2.2)	4.0 (3.6)	2.4 (0.5)	81 (57.9)	797.4 (300.7)	9.2 (4.1)
	<6	151	64.0 (9.4)	5.1 (1.9)	6.2 (1.8)	1.5 (1.1)	2.4 (0.5)	95 (62.9)	612.5 (319.0)	3.4 (1.4)
	≥6	114	65.2 (8.1)	11.0 (4.3)	6.2 (2.3)	4.4 (3.6)	2.4 (0.5)	65 (57.0)	812.2 (295.5)	10.1 (4.1)
	<7	174	64.1 (9.2)	5.4 (2.0)	6.2 (2.0)	1.6 (1.2)	2.4 (0.5)	108 (62.1)	631.5 (316.8)	3.8 (1.6)
	≥7	91	65.3 (8.0)	11.9 (4.2)	6.2 (2.1)	4.9 (3.8)	2.5 (0.5)	52 (57.1)	826.3 (293.8)	11.0 (4.1)
	<8	190	64.2 (9.1)	5.7 (2.2)	6.3 (2.1)	1.7 (1.4)	2.4 (0.5)	117 (61.6)	649.8 (314.0)	4.1 (1.8)
	≥8	75	65.3 (8.0)	12.5 (4.3)	6.0 (2.0)	5.2 (3.9)	2.4 (0.6)	43 (57.3)	821.4 (311.4)	11.8 (4.1)

Rows shaded in grey indicate variables generally associated with earlier disease course (i.e. lower L-dopa duration of use), in comparison with matched unshaded rows.
H&Y, Hoehn and Yahr; L-dopa, levodopa; MF, motor fluctuations; OPC, opicapone; PD, Parkinson's disease; SD, standard deviation.

Table 2. Efficacy of OPC 50 mg and difference versus PLC in specific subgroup analyses (FAS)

		N	Change from baseline in OFF-time (mins) LS Mean (SE)	Δ vs PLC (SE)	p-value
L-dopa duration (years)	<4	96	-107.8 (15.9)	**-43.2 (23.4)**	0.0070
	≥4	166	-121.7 (12.4)	-58.8 (16.6)	0.0004
	<5	124	-107.9 (13.9)	**-47.8 (20.2)**	0.0008
	≥5	138	-124.6 (13.5)	-55.0 (18.1)	0.0024
	<6	149	-113.4 (12.7)	**-62.7 (17.9)**	0.0005
	≥6	113	-120.5 (14.9)	-55.0 (20.4)	0.0072
	<7	171	-122.8 (11.9)	**-73.0 (16.7)**	<0.0001
	≥7	91	-104.0 (16.6)	-33.7 (22.5)	0.1352
	<8	187	-122.2 (11.4)	**-70.8 (15.9)**	<0.0001
	≥8	75	-101.7 (18.3)	-30.0 (25.0)	0.2309

Rows shaded in grey indicate variables generally associated with earlier disease course (i.e. lower L-dopa duration of use), in comparison with matched unshaded rows. Values shown in bold indicate variables for which the difference in change from baseline in OFF-time for OPC 50 mg versus PLC (Δ vs PLC) was greater than that of the matched comparative row; H&Y, Hoehn and Yahr; L-dopa, levodopa; LS, least square; OPC, opicapone; PD, Parkinson's disease; PLC, placebo; SE, standard error.

Table 3. Pooled safety data in specific OPC 50 mg subgroup analyses (Safety Set)

		N	Any TEAE, n (%)	Any related TEAE, n (%)	Incidence of related TEAEs (dopaminergic-related), n (%) Dyskinesia	Nausea	Hallucination	Orthostatic hypotension	Vomiting
L-dopa duration (years)	<4	97	58 (60%)	30 (31%)	11 (11%)	3 (3%)	5 (5%)	1 (1%)	1 (1%)
	≥4	168	112 (67%)	83 (49%)	43 (26%)	5 (3%)	4 (2%)	5 (3%)	4 (2%)
	<5	125	77 (62%)	44 (35%)	13 (10%)	4 (3%)	4 (3%)	2 (2%)	1 (1%)
	≥5	140	93 (66%)	69 (49%)	41 (29%)	4 (3%)	5 (3%)	4 (3%)	4 (3%)
	<6	151	90 (60%)	52 (34%)	15 (10%)	4 (3%)	6 (4%)	2 (1%)	1 (1%)
	≥6	114	80 (70%)	61 (54%)	39 (34%)	4 (4%)	3 (3%)	4 (4%)	4 (4%)
	<7	174	104 (60%)	61 (35%)	21 (12%)	4 (2%)	6 (3%)	2 (1%)	1 (1%)
	≥7	91	66 (73%)	52 (57%)	33 (36%)	4 (4%)	3 (3%)	4 (4%)	4 (4%)
	<8	190	117 (62%)	70 (37%)	28 (15%)	4 (2%)	6 (3%)	3 (2%)	1 (1%)
	≥8	75	53 (71%)	43 (57%)	26 (35%)	4 (5%)	3 (4%)	3 (4%)	4 (5%)

Rows shaded in grey indicate variables generally associated with earlier disease course (i.e. lower L-dopa duration of use), in comparison with matched unshaded rows; L-dopa, levodopa; OPC, opicapone; TEAE, treatment-emergent adverse event (preferred term shown for dopaminergic TEAEs)

Conclusion: These findings indicate that there may be an added benefit from using OPC 50 mg as a first-line adjunctive therapy to levodopa and promptly in the motor fluctuations spectrum of PD.
Disclosure: 1.Ferreira et al., Lancet Neurol. 2016;15(2):154-165; 2.Lees et al., JAMA Neurol. 2017;74(2):197-206

EPR-050

MiR-126-3p as a potential biomarker for Parkinson's disease

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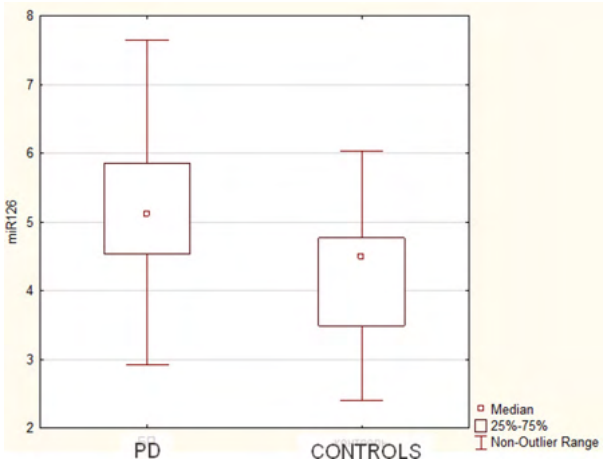
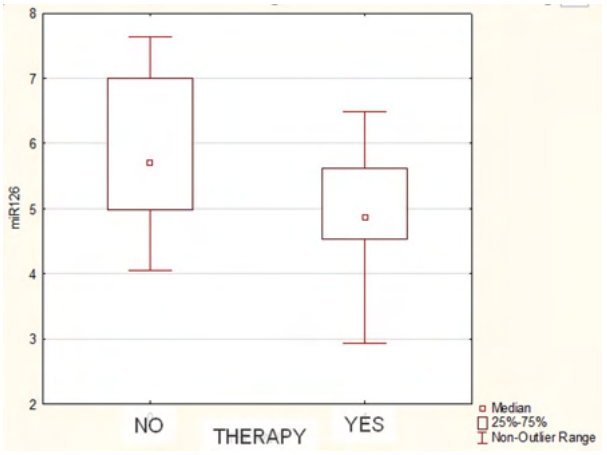
Background and aims: Most of Parkinson's disease (PD) cases have multifactorial etiology. One of the possible mechanisms involved in the pathogenesis of PD is epigenetic regulation of gene expression. MicroRNA, as one of the epigenetic regulators, showed differential expression in PD and control groups in various tissues, particularly in the blood. The aim of our study was to analyze the role of microRNA as a potential biomarker of PD.

Methods: We examined 40 patients with PD and 20 healthy controls. Expression of miR-7-5p, miR-132-3p, miR-146a-5p, miR-106a-5p, miR-29a-3p, miR-221-3p, miR-30c-1-5p and miR-126-3p was measured in the blood leukocytes using reverse transcription, followed by real-time PCR. Data analysis was performed with Statistica 10.0.

Results: A significant difference in the expression of miR-126-3p was found between PD (5.19±1.02) and the control group (4.18±0.92) (t-test, p=0,0004). We observed weak but significant negative correlations of miR-126-3p expression with the disease duration (r=-0.38) and the Hoehn-Yahr stage (r=-0.35). MiR-126-3p also showed differential expression in the groups of drug-naïve patients (5.83±1.18) and patients on antiparkinsonian therapy (4.96±0.87) (t-test, p=0.014).



MiR-126-3p level is higher in PD group



MiR-126-3p level is higher in group without therapy

Conclusion: miR-126 could be a potential biomarker for PD and its expression changes with treatment.

Disclosure: Funding: The study was supported by the Russian Science Foundation, grant #17–75–20211.

EPR-051

Essential tremor: What is beyond the oscillatory monosymptomatic illness?

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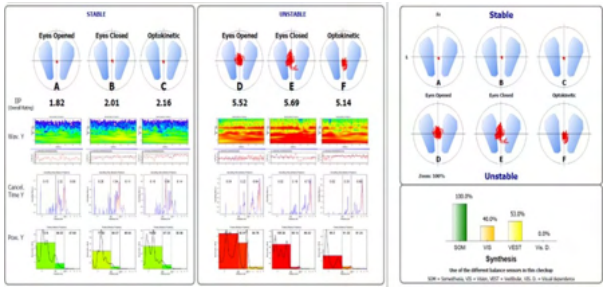
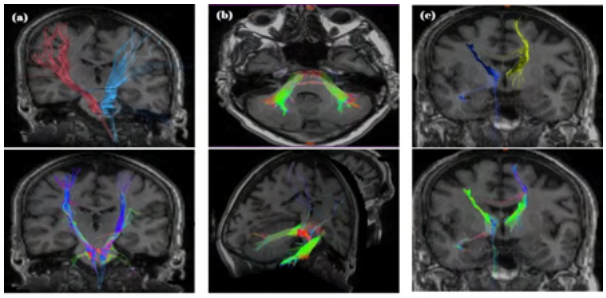
Background and aims: Essential tremor (ET) is now considered as a slowly progressive neurodegenerative disorder with a variety of motor and non-motor manifestations. The objectives of this work were to study the existence of cognitive, mood, olfactory, and balance dysfunctions in ET patients and their relation to tremor severity as well as patients' activity of daily livings.

Methods: This study was performed on 36 ET patients and 24 healthy controls subjects (HCS) submitted to The Essential Tremor Rating Assessment Scale (TETRAS), advanced activity of daily living scale (AADLs), Montreal cognitive assessment scale (MoCA), Montgomery–Åsberg Depression Rating Scale (MADRS), auditory mismatch negativity (MMN), Sniffin' Sticks test (SST), computerized dynamic posturography (CDP) and brain MRI diffusion tensor tractography (DTT).

Results: ET patients showed a significant decrease in AADLs, MoCA, SST (threshold, identification, and discrimination subscales) as well as visual and vestibular ratios of CDP compared to HCS. Auditory MMN showed a significant reduction in the amplitude and prolongation of latencies while Corticospinal tracts, thalamocortical connectivity, and middle cerebellar peduncles DTT revealed reduced fractional anisotropy in ET patients with normal tracts densities.





CST	Right	Left
Minimum FA	0.281	0.243
Maximum FA	0.912	0.934
Mean FA	0.469	0.462
Tract density	402	389

MCP	Right	Left
Minimum FA	0.341	0.264
Maximum FA	0.943	0.894
Mean FA	0.462	0.493
Tract density	834	468

TCC	Right	Left
Minimum FA	0.207	0.224
Maximum FA	0.897	0.824
Mean FA	0.334	0.348
Tract density	892	720

Conclusion: ET patients exhibit a wide variety of non-motor manifestations including cognitive impairment, depressive symptoms, hyposmia, and increased risk of falls with consecutive reduced activity of daily living beyond the deleterious effects of the kinetic tremor.

Disclosure: Nothing to disclose.

EPR-052

Anodic and biphasic pulses give larger therapeutic windows than cathodic pulses in essential tremor patients

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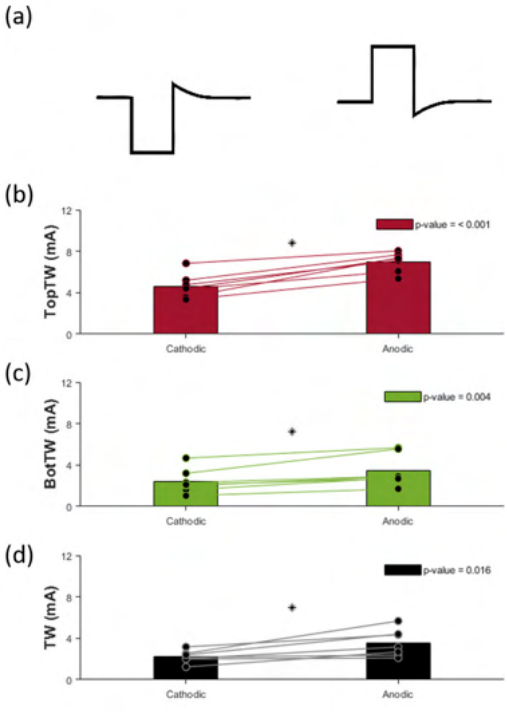
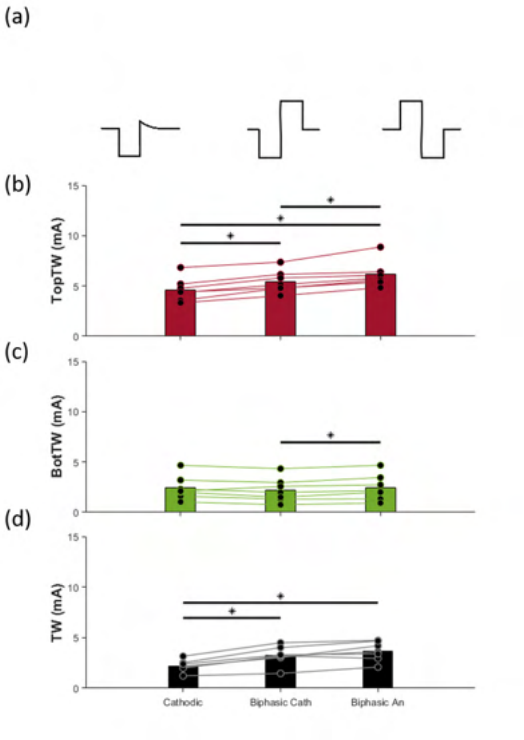
Background and aims: Medication refractory essential tremor (ET) can be successfully treated with deep brain stimulation (DBS). However, in a significant number of patients the stimulation amplitude needed for tremor arrest will increase over time and approach the stimulation amplitude that causes side-effects. This results in a narrow therapeutic window (TM), rendering DBS therapy ineffective.

Methods: A randomized, doubled-blinded, cross-over design was used to test the effect of cathodic, anodic pulses and biphasic pulses (cathode-first and anode-first) on TW in an acute clinical setting in six ET patients (7 hemispheres). TW was defined on the lower end by intention tremor arrest and on the upper end by stimulation-induced side effects.

Results: Anodic stimulation gave a significantly larger TW compared to cathodic stimulation (p=0.016). Biphasic stimulation also increased TW compared to cathodic stimulation for both cathode-(p=0.002) and anode-first (p<0.001) biphasic pulses. For both anodic and biphasic pulses, the effect on TW was mainly driven by an increase in the side-effect threshold. The order of the phases in the biphasic pulse has a significant effect on the BotTW and the TopTW. All pulses were safe and well-tolerated.



Results of therapeutic window in cathodic versus anodic stimulation



Results of therapeutic window in cathodic versus biphasic stimulation

Conclusion: Anodic and biphasic pulses can increase TW in ET patients. This effect could be clinically useful in ET patients where DBS has become ineffective because of a narrow TW.

Disclosure: Nothing to disclose.

MS and related disorders 1

EPR-053

Proteomic profiling for novel biomarkers of risk of conversion to multiple sclerosis and of disease severity

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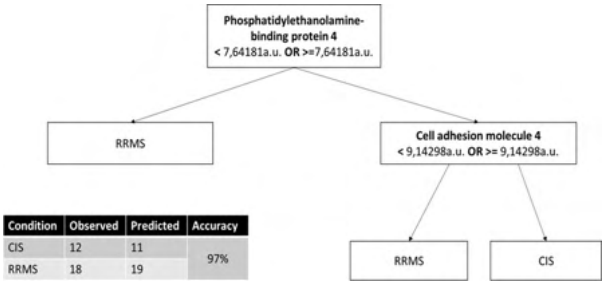
Background and aims: Multiple sclerosis (MS) affects more than 2.5 million people worldwide. It frequently begins by a first clinical episode that may not fulfil the criteria of MS and may remain isolated (clinically isolated syndrome [CIS]). There is thus a need for more sensitive and specific biomarkers to improve diagnostic and prognostic accuracy early in the course of the disease, to tailor treatment to patients' individual risk. Sequential Window Acquisition of all Theoretical fragment-ion spectra mass spectrometry (SWATH-MS) method offers unsurpassed proteomic coverage and more reproducible quantification.

Methods: Clinical data were retrospectively collected. We use the SWATH-MS strategy on leftover CSF samples collected at initial presentation in a population of 12 CIS and 18 RRMS patients followed in our Neurology Department (mean follow-up duration: 31 months). Proteins of interest were selected on the basis of the quality of their peptide identification (peak-detection q-value<0.01) and dysregulation between both groups (fold-change adjusted p-value<0.05). We used Random Forest Classification (RFC) to elaborate a mean classification tree for CIS and RRMS.

Results: Clinical features are summarized in Table. SWATH-MS analysis identified 820 proteins, of which 101 were selected for RFC based on our pre-specified criteria. A mean classification tree (Figure) was obtained using Cell adhesion molecule-4 and Phosphatidylethanolamine-binding protein-4 with an overall accuracy of 97%.

Clinical Characteristics	Whole cohort	CIS	RRMS	P value
Number of patients (n)	30	12	18	
Age (years)*	30.5 (10.7)	30.5 (7.5)	30.5 (12.5)	0.98404
Female/male (% female)	21/9 (70%)	9/3 (75%)	12/6 (67%)	0.7036
Months of follow up*	31 (14.9)	27 (17.4)	32 (12.5)	0.35238
Initial clinical presentation				
Optic Neuritis	8 (27%)	7 (58%)	1 (6%)	0.0025
Brain stem	4 (13%)	3 (25%)	1 (6%)	0.2742
Spinal	15 (50%)	2 (17%)	13 (72%)	0.0078
Others	3 (10%)	0	3 (17%)	0.2552
Total protein (mg/dL)*	28 (6.4)	27 (7.4)	30 (5.8)	0.25428
Presence of OligoClonal Bands (OCB)	25 (83%)	7/12 (58%)	18/18 (100%)	0.0056
Number of White Cells/mm^3*	3 (11.4)	3 (5.6)	2.5 (7.4)	0.254

Table: Clinical information and CSF characteristics of the cohort by subgroups; CIS Clinically Isolated Syndrome, RRMS Relapsing Remitting Multiple Sclerosis. *Data are expressed as mean ± standard deviation.



Condition	Observed	Predicted	Accuracy
CIS	12	11	97%
RRMS	18	19	

Figure: the diagram represents the mean decisional tree of the Random Forest Classification to RRMS or CIS. Results are expressed in Area Under the Curve (a.u.). The table resumed the observations and the accuracy of the decisional tree.

Conclusion: SWATH-MS analysis is a promising tool to investigate the proteomic of CIS and MS. These preliminaries data need to be validated in a larger and independent cohort.

Disclosure: No disclosure to declare

EPR-054

School performance, psychiatric comorbidity, and healthcare utilization in pediatric multiple sclerosis

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Background and aims: Pediatric multiple sclerosis (MS) may hamper educational achievements due to psychiatric comorbidity and cognitive impairment. Our aims were to investigate school performance, psychiatric comorbidity and healthcare utilization following pediatric MS and to differentiate between disability in MS and that arising from a non-brain-related chronic disease.
Methods: We included all children (<18 years) with MS onset during 2008–15 in Denmark with a medical record-validated MS diagnosis. The control groups were children from the general population or children with non-brain-related chronic diseases. Outcomes were register-based on 9–12 grade point average, psychiatric comorbidity, and healthcare visits.
Results: Cohorts were children with MS (n=92), control children matched to children with MS (n=920), children with non-brain-related chronic diseases (n=9,108), and "healthy" children with neither MS nor brain-related chronic disease (n=811,464). School performance in grades 9–12 was similar, but children with MS compared with those with non-brain-related chronic disease had an almost doubled hazard for psychiatric comorbidity (hazard ratio=1.87; 95% confidence interval=1.382.53; p<0.0001) and a higher rate of all hospital visits (p<0.0001) but a lower rate of hospital admissions (p=0.001).
Conclusion: Children with MS have a seemingly standard school performance but increased psychiatric comorbidity and a high rate of healthcare utilization.
Disclosure: Dr. Boesen has served on a scientific advisory board for Teva has received speaker honoraria for lecturing from Novartis, and support for congress participation from Teva, Novartis and Roche.

EPR-055

Peak width of Skeletonized Mean Diffusivity (PSMD) as a reliable marker of neuropsychological performance in RRMS

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Background and aims: PSMD, as a novel marker of white matter microstructure damage, is associated with cognitive decline in several white matter conditions (i.e. small vessel disease and CADASIL). We hypothesized that an alteration in WM could be associated with clinical disability, especially cognitive dysfunction in RRMS patients.
Methods: We used peak width of skeletonized mean diffusivity (PSMD) based on Tract-based Spatial Statistics (TBSS) of diffusion tensor imaging MRI scans. We investigated RRMS patients (n=79) treated on IFN- therapy. The clinical and neuropsychological data in the cross-sectional study was correlated with the PSMD parameter.

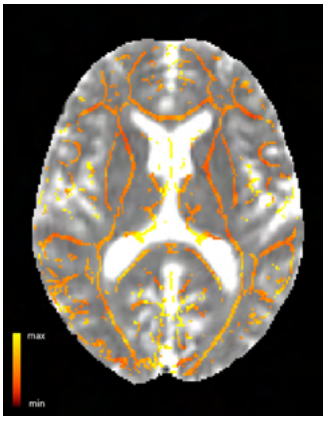

Fig.1 Examples MD of an RRMS patient projected onto a standard skeleton obtained with Tract-Based Spatial Statistics of diffusion tensor imaging. Mean diffusivity with superimposed skeletonized tracts

Results: Spearman's analysis exhibited a significant correlation between PSMD and cognitive function, especially processing speed and attention in SDMT (rho= -0.43, p<0.0001), CCT1 time (rho=0.32, p<0.05) and CCT2 time (rho=0.37, p<0.001), disability level EDSS (rho= 0.243, p<0.05), and upper arm function, 9-HP test (rho= -0.367, p<0.001)
Conclusion: These findings point out that PSMD may be a relevant marker of cognitive decline and physical disability in RRMS. The fact that PSMD is a fully automated and objective method raises the opportunity for its wider application for further research in clinical trials and everyday practice. PSMD can supplement routine MRI studies to be used as a reliable radiological marker of cognitive dysfunction, resulting in early treatment interventions.
Disclosure: No conflicts of interest to declare.

EPR-056

Improvements in Work Productivity and Activity Impairment in OCR-treated patients with RRMS: 2-year CASTING study data

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Background and aims: The Work Productivity and Activity Impairment (WPAI) questionnaire is a patient-reported outcome assessing percentage of work time missed, impairment while working, overall work impairment and activity impairment over seven days prior. We report 2-year changes in WPAI, and associations with the 29-item Multiple Sclerosis Impact Scale (MSIS-29) and SymptoMScreen (self-reported symptom burden) among patients with relapsing-remitting MS (RRMS) in the Phase IIIb CASTING trial (NCT02861014).
Methods: Patients (n=680; Expanded Disability Status Scale score ≤4.0) with a suboptimal response to one or two prior disease-modifying therapies (DMTs) received intravenous ocrelizumab 600mg every 24 weeks for 96 weeks. WPAI, MSIS-29 and SymptoMScreen were completed at baseline, Week 24, Year 1 and Year 2. Spearman correlations were assessed between change in WPAI subscores from baseline to Year 2, MSIS-29 subscores, and SymptoMScreen total score.
Results: WPAI improved from baseline to Year 2, with significant reduction in overall work impairment (-3.08, p=0.020) and activity impairment (-5.69, p<0.001), and consistent trends in work time missed (-2.54, p=0.102) and impairment while working (-1.66, p=0.129). Improvement in SymptoMScreen score correlated with reduction in all WPAI measures: work time missed (rs=0.196), impairment while working (rs=0.387), overall work impairment (rs=0.362) and activity impairment (rs=0.421) over two years (all p<0.01). MSIS-29 improvements correlated with WPAI improvements over two years (Table 1).

WPAI subscore	MSIS-29 (correlation coefficient r_s)	
	Physical	Psychological
Work time missed	0.181, p=0.001	0.198, p<0.001
Impairment while working	0.457, p<0.001	0.361, p<0.001
Overall work impairment	0.386, p<0.001	0.343, p<0.001
Activity impairment	0.524, p<0.001	0.384, p<0.001

Table 1

Conclusion: Patients with a suboptimal response to one or two prior DMTs who switched to ocrelizumab showed improvement in work productivity (WPAI), which correlated with improvement in physical/psychological impacts of MS (MSIS-29) and decrease in symptom burden (SymptoMScreen) over two years.
Disclosure: Sponsored by F. Hoffmann-La Roche Ltd; writing and editorial assistance was provided by Articulate Science, UK.

EPR-057

Real-World Clinical and Patient-reported Effectiveness of Dimethyl Fumarate is Maintained Over four Years: PROTEC Substudy

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Background and aims: Dimethyl fumarate (DMF) demonstrated a favorable benefit-risk profile in Phase 3 studies of patients with multiple sclerosis (MS). PROTEC, an international phase 4, open-label, observational study assessed real-world effectiveness of DMF on disease activity and patient reported outcomes (PROs). The objective was to report 4-year effectiveness of DMF from an extension sub-study of Portuguese participants in PROTEC.
Methods: In the sub-study, eligible participants continued taking DMF following the 12-month main study, for up to 48 months. The primary objective was to estimate ARR over 48 months. Additional endpoints were patient-reported health related quality of life (HRQoL) outcomes, disability progression, depression/mental health, and work productivity outcomes.
Results: A total of 1,114 patients were enrolled in PROTEC; 134 (12.0%) were Portuguese and, of those, 103 (76.9%) enrolled in the extension study. 71 (68.9%) participants completed the extension study while 32 (31.1%) withdrew early; four (3.9%) participants discontinued due to AEs. ARR was 0.447 (95% CI: 0.331, 0.603) at Baseline, decreased to 0.146 (95% CI: 0.085, 0.249) at Month 12 of treatment, 0.116 (95% CI: 0.074, 0.183) at Month 24, and 0.118 (95% CI: 0.079, 0.176) at Month 48. Nearly 74% of participants experienced no relapses by Month 48. Over the 48 months follow up, participants generally showed improvement or stabilization vs baseline across patient-reported measures of HRQoL, health status, disability progression, and work productivity.
Conclusion: DMF is an effective treatment for MS patients, from both a clinical and patient perspective for long-term quality of life, health status, and disability progression.
Disclosure: AMS has received compensation as a speaker and for consulting, clinical trial research, and advisory board participation from Biogen, Bayer, Merck Serono, Teva, Novartis, Roche, and Sanofi-Genzyme. JB, FB, CF, and JL are employees of Biogen.

EPR-058

Head circumference in newborns of Multiple Sclerosis mothers and risk of macrocephaly

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Background and aims: There are some controversies about the neonatal anthropometric measures of infants born to MS mothers. Applying WHO standards, some studies reported an increase of head circumference at birth which has been associated with neurodevelopmental disorders.
Methods: Prospective study in pregnant women and their newborns. Gestational age and head circumference (HC) were analyzed applying WHO and Olsen curves and Orbegozo-Foundation references standards.
Results: We studied 76 women and 96 pregnancies, 90 deliveries and six still ongoing. Mean maternal age was 35±4 years. After excluding preterm and posterm, we analyzed head circumference of 83 term newborns, 45 girls and 38 boys and mean gestational age of 39.4±1. Male infants mean HC at birth was 34.8cm±1,28 compared with WHO 50th percentile reference of 34.5cm (p=0.07). Female mean birth HC was 34.6cm±0,99, larger than WHO reference of 33.9 cm ($p<0.05$). Applying Olsen et al. growth curves, worldwidemost accepted charts in neonatal centers, that include gender-specific HC-for age curves we do not find statistically differences between our cohort and Olsen curves.Comparing our cohort and 50th percentile of the Orbegozo-Foundation curves, based on Spanish population, there were no significant findings (Table 1).

Head circumference				
Male				
Weeks	Our cohort	Olsen	Orbegozo	WHO
All term	34,9 ± 1,3		34,8 ±1,2 (p0.632)	34,5 ±1.3 (p0.064)
37w	34,5 ± 0,71	33,8 ± 1,7 (p0.560)		
38w	34,4 ± 1,16	34,4 ± 1,7 (p1.000)		
39w	35,3 ± 1,47	34,6 ± 1,6 (p0.115)		
40w	34,8 ± 1,00	34,8 ± 1,5 (p1.000)		
41w	35,0 ± 1,55	35,1 ± 1,5 (p0.870)		
Female				
Weeks	Our cohort	Olsen	Orbegozo	WHO
All term	34,5 ±0,99		34,2 ±1,3 (p0.139)	33,9 ±1.2 (p0.001)
37w	33,8 ± 1,15	33,3 ± 1,7 (p0.177)		
38w	34,4 ± 0,74	33,8 ± 1,6 (p0.205)		
39w	34,7 ± 1,11	34,0 ± 1,5 (p0.140)		
40w	34,3 ± 0,95	34,2 ± 1,5 (p0.825)		
41w	35,3 ± 0,94	34,5 ± 1,5 (p0.192)		
Data were expressed as mean ± SD for continuous variables. p values are calculated by paired-samples *t*-test. Significance level: p<0.05.				

Table 1. Comparison of gender-specific head circumference-for-age data in our cohort with Olsen charts and mean no specific-age with WHO and Orbegozo 50th percentile.

Conclusion: Applying the adequate charts for every population, and gestational age standards, mean HC at birth in newborns of MS mothers do not differ from newborns of healthy mothers, therefore they do not have macrocephaly. In order to compare anthropometric measurements in newborns it is crucial to apply standards references that include sex, gestational age and if possible national growth standards to avoid bias.
Disclosure: Nothing to disclose.

EPR-059

The expression and clinical correlation analysis between RGMa and neuromyelitis optica spectrum disorders

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Background and aims: This study aims to explore the expression of Repulsive Guidance Molecule a (RGMa) in neuromyelitis optica spectrum disorders (NMOSD) and to explore the correlation between RGMa and the clinical features of NMOSD.
Methods: 54 NMOSD patients and 22 age-matched healthy control (HC) patients were enrolled from October 2017 to January 2020. Clinical data were collected and the expression of serum RGMa was detected by enzyme linked immune-assay (ELISA). Then the relations between the RGMa expression level and the demographic features, EDSS score, degree of MRI enhancement, and AQP4 titer were analyzed by Pearson and Spearman correlation analysis.
Results: 54 cases of NMOSD patients were composed of 14 males and 41 females. For the expression of RGMa, the NMOSD group was higher than the HC group ($p<0.001$), the acute phase group was higher than the remission group ($p<0.001$), the AQP4 positive group was higher than the AQP4 negative group ($p<0.05$). A positive correlation was discovered between RGMa expression in NMOSD and EDSS score or degree of MRI enhancement, segmental length of spinal cord lesions, AQP4 titer respectively ($p<0.001$). There was a negative correlation between expression of RGMa and delta EDSS score ($p<0.001$).
Conclusion: The expression and clinical correlation analysis between RGMa suggested that RGMa may be considered as a potential biomarker for predicting the severity and clinical features of NMOSD. RGMa probably involved in the pathogenesis of NMOSD but further study needs to be explored.
Disclosure: Data within this article is not published.

Neurotoxicology/occupational neurology

EPR-060

Contrast Induced Encephalopathy – A Diagnosis That Should Not Be Overlooked

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Background and aims: Digital substraction angiography of the cervical-cerebral arteries (DSA-CCA) represent a part of the daily intervention practice and is widely performed. One rare complication is contrast induced encephalopathy (CIE). CIE is defined as a reversible neurological syndrome during/after a procedure in which a large volume of contrast is used. Neurological deficits are related to the involved hemisphere.
Methods: We present a series of two patients: a 63-year-old female with a symptomatic left carotid artery stenosis of 70% and a 69-year-old male with an aneurysmal dilation of 23/15mm in the proximal part of the basilar artery.
Results: At hospital admission, patients had no neurological deficits. They underwent DSA-CCA and endovascular treatment with carotid stenting and basilar aneurysm stenting and coiling. During the procedure the female developed right hemiplegia, right facial palsy, aphasia and the male patient developed delirium and cortical blindness. The intracranial angiography didn't detect any vascular abnormalities. The postprocedural CT scans revealed marked contrast enhancement „staining" of the left hemisphere in the case of the female patient and of the bilateral occipital-parietal lobes of the male patients. The neurological deficits resolved within 24 hours.
Conclusion: CIE is an infrequent transient neurotoxic effect of the iodinated contrast during angiography, but it must be differentiated from other procedural complications to avoid unnecessary measures that may affect the patient's outcome. Although CIE has a good prognosis, future contrast interventions should be undertaken with caution.
Disclosure: Nothing to disclose.

EPR-061

Visual perception disturbances in ozone encephalopathy.

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Background and aims: Ozone has been increasingly used as treatment for arteritis, lumbar disc herniation, ischemic heart disease, stroke and cancer. Adverse effects have been rarely described, particularly in CNS, which the most frequent are headache and nausea.
Methods: We report a rare case of ozone encephalopathy.
Results: A 67-year-old right-handed woman with a history of bilateral carpal tunnel syndrome undergoing ozone therapy was admitted with severe headache and transient loss of consciousness, followed by behaviour and language disturbances starting immediately after ozone therapy session (30ppm, subcutaneous local administration). Her blood pressure was normal. Neurological examination disclosed an attention impairment, transcortical motor aphasia and cortical blindness. Blood and CSF tests were normal. Brain-CT, angio-CT, MRI and EEG were unremarkable; After 24 hours, she presented multiple visual perception phenomena: prosopometamorphopsia, macropsia, kinetopsia and macrosomatoagnosia, suggestive of "Alice in Wonderland syndrome", as well as severe impairment of recent episodic memory. Brain-MRI at 48-hours showed diffuse occipital white-matter FLAIR/T2 hyperintensities and DWI hyperintensities in both hippocampi. Neuropsychological evaluation at the 7th-day documented deficits in attention, episodic verbal and visual memory and associative prosopagnosia. She progressively improved. However, the neuropsychological re-evaluation after 8-months still showed a moderate deficit in recent verbal episodic memory and a marked semantic memory deficit.
Conclusion: This case of ozone encephalopathy shares clinical and imagiological features with posterior reversible encephalopathy syndrome (PRES). Allthough the molecular mechanisms associated with ozone toxicity remain poorly understood, three previous cases of cortical blindness were reported, with similar imaging pattern and reversibility.
Disclosure: Nothing to disclose.

EPR-062

Low Voltage Electrocution Brain Injury

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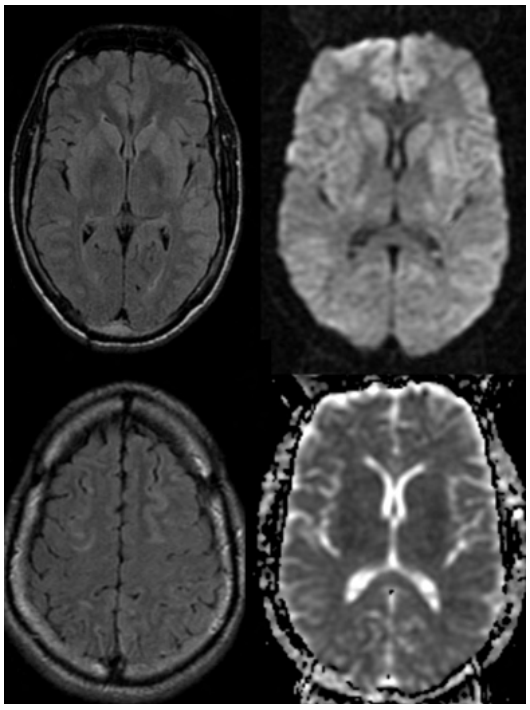
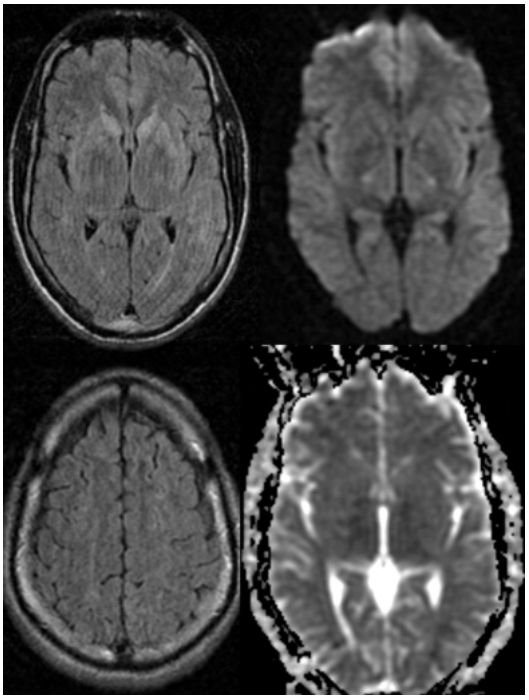
Background and aims: Electrocution injuries can affect different organs. The literature on clinical/laboratory/therapeutic characteristics of the central nervous system (CNS) is scarce. Direct thermal effect of the current, ionic deregulation resulting from the electroporation of cell membranes and hypoxic-ischemic context are possible mechanisms.

Methods: A 31-year-old man without past medical history underwent low-voltage electrocution. This resulted in cardiorespiratory arrest that was reversed within 15 minutes. After sedation withdrawn, the patient presented psychomotor agitation, global aphasia and choreiform orofacial movements. Cerebral tomography was normal. The electroencephalogram revealed diffuse slowing with left temporal predominance, without paroxysmal activity. After 5-days, brain MRI was performed revealing areas of cortical hypersignal in T2-FLAIR without diffusion restriction mainly on the left frontal-temporo-parietal lobes and basal ganglia (BG) (figure-1). 30mg haloperidol were required for behavioral control (also reversing choreiform movements). Thinking that the lesions could correspond to cerebral edema, five days of 1g of methylprednisolone were performed. After the third day there was a progressive clinical improvement. The post corticotherapy brain MRI revealed a marked decrease in hypersignal areas (figure-2).



Bilateral hypersignal in T2 FLAIR with predominance of left temporo-parieto-temporal lobes, caudate nuclei and putamine.



Reduction of the hypersignal in T2 FLAIR of putamine, persisting a slight hypersignal of the caudate nuclei. Reversion of the cortical hypersignal in the high convexity bilaterally seen in fig.1, suggesting a decrease in the local inflammatory process.

Results: Currently he is in rehabilitation. Can carry out orders, independent in walking, hygiene and food intake. Still maintains akinetic mutism possibly due to BG's sequelae injury.

Conclusion: CNS injuries after electrocution can occur at several levels, so the clinical picture can be very heterogeneous. In this case, it was dominated by neuropsychiatric and movement changes. Corticotherapy was an important step towards clinical improvement and reversal of imaging findings, assuming that there was a contribution of inflammatory edema in the lesions.

Disclosure: Nothing to disclose.

EPR-063

Peripheral nervous system involvement in glue-sniffers : a case series

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Background and aims: Voluntary N-hexane intoxication is common in young adults and is reponsible for a large spectrum of peripheral nervous system involvement. The functional outcome may be poor even after withdrawal. Here we present a case series of nine glue-sniffers who presented with various peripheral nervous system manifestations.
Methods: Patients with a history of voluntary chronic n-hexane intoxication were included. Cerebrospinalfluid (CSF) examination, electrophysiological findings and follow up are reported.
Results: All patients were male with a mean age of 23,33 ±12,43 years. Mean intoxication time was of 12.3 years [1–35 years]. Seven out of nine patients presented with an acute/rapidly progressive onset two of which mimicking a Guillain-Barré syndrome. Electrophysiological patterns were heterogenous: a chronic inflammatory demyelinating polyneuropathy (CIDP)was assigned for in three cases, a sensory motor polyneuropathy in five cases, mostly demyelinating ; a non traumatic brachial plexus injury in one patient. Two patients had an asymmetrical distribution. CSF findings were unremarkable except for one case with albumino-cytologic dissociation. Four patients improved spontaneously after withdrawal. one patient worsened. Both patients with an acute polyradiculoneuropathy did not remarkably benefit from intravenous immuno-globulintherapy (IV IgG). One patient with CIDP had frequent relapses but benefited from a trimestrial IV IgG regimen.
Conclusion: N-hexane related neuropathy is usually of subacute onset but an acute onset is not exceptionnal and might masquerade as a Guillain Barré syndrome. The most common clinical and electrophysiological pattern is a sensory-motor polyneuropathy. Neurological manifestations and outcome after withdrawal depend on the dose and duration of the intoxication.
Disclosure: Authors declare no conflicts of interest.

EPR-064

Demographic variables of psychostimulant and hypnotic-sedative intoxication in Brazil

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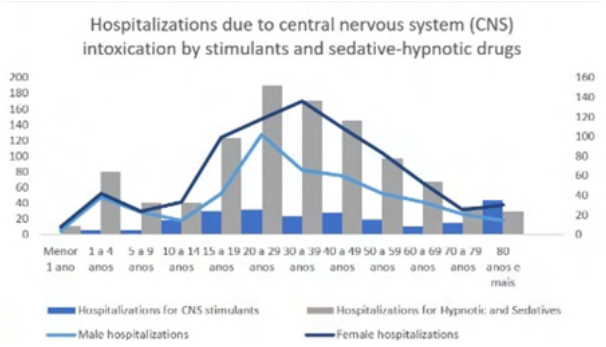
Background and aims: Psychostimulants, mostly used by students and adults, are a recurrent cause of hospital emergency demand, and can lead to dependence and intoxication with its adverse effects. Hypnotic-sedative drugs are essentially used to fight insomnia and anxiety disorders. This study aims to describe the demographic variables of intoxication by psychostimulant and hypnotic-sedative drugs in Brazil.
Methods: This is an ecological study with secondary data extracted from the brazilian Ministry of Health databases, through DATASUS. The investigated period ranges from December 2009 to December 2019, in Brazil. The data refers to the use of hypnotic-sedative, tranquilizer, and stimulant Central Nervous System drugs. The variables explored were: age range, sex, colour and number of hospitalizations.
Results: There were 1,219 cases, 84.4% of which refer to sedatives-hypnotic drugs and tranquilizers. There was a predominance of 20–49 year old people hospitalized for both drugs, corresponding to 49.5% of the cases. Furthermore, females accounted for 64.8% of intoxications by sedatives-hypnotics and tranquilizers, whilst for neurostimulants there was an equal prevalence for both sexes. Regarding both drug classes, white and brown people represent 62.9% of hospitalized patients, while black count for 6%.



Graph 1 - Hospitalizations due to central nervous system intoxication by stimulants and sedative-hypnotic drugs.

Conclusion: There was a predominance of psychostimulant and sedatives used by individuals between 20 and 49 years old, due to the search for better cognitive performance and quality of sleep, which can foment the abusive consumption of these substances. Moreover, the prevalence of hypnotic-sedative drugs hospitalizations in the female population may be related to the higher rate of anxiety disorders in this group.
Disclosure: Nothing to disclose.

COVID-19 1

EPR-065

Rate of critical illness neuromyopathy during the first wave of COVID-19 pandemic: a single center retrospective study

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Background and aims: Critical illness myopathy and/or neuropathy (CRIMYNE) is the most common cause of intensive care unit acquired weakness (ICUAW). The incidence varies widely depending on diagnostic criteria, underlying disease and timing of evaluation. Our aim was to evaluate the rate as well as clinical and neurophysiological features of CRIMYNE in ICU patients of San Raffaele Hospital (Milan) during the first wave of COVID-19 pandemic.
Methods: CRIMYNE diagnosis among ICU patients of our Institute between January and June 2020 were retrospectively collected. As a control population, CRIMYNE diagnosed in the same interval of 2019 and 2018 were considered. Based on neurological examination and electrophysiological testing, we attempted to distinguish critical illness neuromyopathy (CINM) from polyneuropathy (CIP) and myopathy (CIM).
Results: The overall rate of CRIMYNE diagnosis during the first half of 2020 was 6.8% (19 out of 276 patients). When considering COVID-19 positive cases, the rate increased to 9.3% (vs 4.7% in COVID-19 negative patients). The rate of CRIMYNE diagnosis in the same months of 2019 and 2018 was 6.9% and 6.1% respectively. In the whole cohort of 2020 as well as in 2019 and 2018 cohort, most patients received CINM diagnosis (42.1%, 50%, 46.1%), about one third CIM diagnosis (36%, 33.3%, 30.7%) and the remaining were diagnosed as CIP (21%, 16.6%, 23%). In COVID-19 positive patients, an increase in CIM diagnosis was observed (58.3%).
Conclusion: This preliminary study shows the relevant increased rate of CRIMYNE in ICU patients with COVID-19, likely due to a more severe whole clinical picture in these patients.
Disclosure: Nothing to disclose.

EPR-066

COVID-19 severity and mortality in multiple sclerosis do not depend on immunotherapy: a nation-wide Austrian registry

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Background and aims: The COVID-19 pandemic challenges neurologists in counseling patients with multiple sclerosis (pwMS) regarding SARS-CoV-2 risk and in guiding disease-modifying treatments (DMT). We aimed to characterize overall mortality and severity of COVID-19 in pwMS and specifically associated with DMT.
Methods: We included pwMS aged 18 years with a confirmed diagnosis of COVID-19 established between January 1, 2020 and December 31, 2020. COVID-19 course was classified as either mild, severe or fatal. Impact of overall and immunosuppressive DMT (alemtuzumab, cladribine, fingolimod, ocrelizumab or rituximab) on probability of severe or fatal COVID-19 was determined by multivariable models, adjusted for a-priori-risk estimated by a recently developed score (comprising age, comorbidities, and degree of disability).
Results: Of 73 MS patients with COVID-19 (mean age: 41.4 years [SD 13.3], 65% female), 87.5% had a mild course, 9.7% a severe course and 2.8% died from COVID-19. A-priori-risk significantly predicted COVID-19 severity (R2 0.862; $p<0.001$) and mortality (R2 0.663; $p<0.001$). Adjusting for a-priori-risk, neither DMT exposure was significantly associated with COVID-19 severity (OR: 1.6; CI: 0.2–11.9; $p=0.667$) or mortality (OR: 0.5; CI: 0.2–19.6; $p=0.711$), nor exposure to specific immunosuppressive DMT (ORs severity and mortality: 1.9 and 2.1; $p=0.426$ and $p=0.233$, respectively).
Conclusion: In a population-based MS cohort, COVID-19 severity and mortality were independent of DMT exposure and immunosuppressive DMT after accounting for unmodifiable risk factors. This provides reassuring evidence that COVID-19 risk can be anticipated in MS and – except for a small proportion of high-risk patients – treatment decisions should be focused on treating MS rather than the pandemic.

Disclosure: Gabriel Bsteh: has participated in meetings sponsored by, received speaker honoraria or travel funding from Biogen, Celgene, Merck, Novartis, Roche, Sanofi-Genzyme and Teva, and received honoraria for consulting Biogen, Roche and Teva.

EPR-067

Cognitive and behaviorial features of a cohort of patients in COVID-19 post-acute phase

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Background and aims: To define post-acute cognitive and behavioural features in a large cohort of subjects with confirmed COVID-19.

Methods: 49 subjects with confirmed COVID-19 underwent a comprehensive neuropsychological assessment and a brain MRI scan within two months from hospital discharge. Frequencies of cognitive and behavioural alterations, according to the normative data, were reported. Total brain volumes were obtained. In all patients, correlations were performed between neuropsychological performances, brain volumes and the severity of acute-phase respiratory symptoms at the time of hospital admission.

Results: At the time of the visit, 16% of patients presented with depressive symptoms and 18% reported post-traumatic stress disorder. 45% of the total sample showed executive dysfunctions, 30% visuospatial difficulties, and 25% long-term verbal and nonverbal memory problems. The youngest patients (age<50) showed the most severe profile with 75% of patients showing executive dysfunctions, 50% pure visuospatial dysfunctions and 40% primary long-term memory problems. The total sample showed a negative relationship between frontal executive performances and the severity of acute-phase respiratory symptoms at the hospital admission ($r=-0.347$; $p<0.01$). No significant relationship was observed between cognitive performances and brain volume.

Conclusion: Cognitive and behavioural alterations are associated with COVID-19 infection within two months from hospital discharge and were more severe in the youngest patients. The patient cognitive/behavioural disturbances were independent of their brain structural integrity. Whether these alterations are directly linked with the infection itself or with its related consequences is still to be determined, as well as whether they are reversible or part of a neurodegenerative process.

Disclosure: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

EPR-068

Prospective EEG evaluation in patients with recent COVID-19 and cognitive disturbances

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Background and aims: Our study aimed to assess EEG findings and their clinical and neuropsychological correlates in patients with recent COVID-19.

Methods: We enrolled 55 adult patients with recent COVID-19, good recovery and objective and/or self-reported cognitive disturbances, observed at follow-up neurological evaluation (2 months after discharge). Same-day basal EEG and neuropsychological testing battery were performed. EEG were assessed for background activity, individual alpha frequency (IAF), presence/location of focal slowing, epileptiform abnormalities and seizures. Correlations with neuropsychological and clinical variables were assessed using linear/logistic regression.

Results: We evaluated 55 patients (70.9% males, mean age 60.5±13.3 years); 13/55 (23.6%) had needed ventilatory support (12 NIV, one intubation). Mean adjusted Montreal Cognitive Assessment (MoCA) score was 21.3±2.8. Modest EEG background-activity alteration was observed in 5/55 (9.1%) patients. Prevailing fronto-temporal focal slow-wave activity (SWA) was observed in 6/55 (10.9%) patients. Brief (<5 sec) anterior theta/alpha activity sequences were recorded in 10/55 (18.2%) subjects. No epileptiform/seizure discharges were recorded. 41/55 (74.5%) patients had experienced mild neurological symptoms during acute-phase COVID-19. Only confusion/disorientation was associated with EEG parameters, particularly with anterior theta/alpha activity. IAF did not correlate with acute-phase respiratory severity scores or neuropsychological findings. Presence of anterior theta-alpha activity was associated with lower executive-function scores at frontal assessment battery and symbol-digit modalities test. Executive-function impairment was not associated with background-activity alteration or SWA.

Conclusion: EEG alterations after COVID-19 might be independent of acute infection severity and suggest a link with ongoing neuro-psychiatric symptoms. Further follow-up data is needed to confirm the reversibility and/or evolution of our findings.

Disclosure: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

EPR-069

Propriospinal myoclonus associated to Sars-Cov-2 respiratory infection

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Background and aims: Propriospinal myoclonus (PM) is an uncommon movement disorder characterized by myoclonic jerks arising in muscles corresponding to a myelomere which spread rostrally and caudally to other myotomes. PM has not been previously reported in the setting of SARS-CoV-2 infection.
Methods: Case report.
Results: A 63 years-old man was admitted to intensive care unit because of severe respiratory SARS-CoV-2 infection. Some infectious complications worsened the clinical course and prolonged the need of mechanical ventilation, without documented respiratory arrest. 40 days after admission to ICU, the patient began to manifest abnormal arrhythmic movements consisting in spontaneous flexion of the trunk, both in abdominal and cervical regions, after withdrawal of sedative drugs. Propofol, fentanyl and midazolam were resumed. Although there was a partial improvement of the movements, they were still present and triggered by auditory or tactile stimuli (Video). An electroencephalogram did not display epileptiform activity. Polymyography showed muscle contractions that started in supraumbilical muscles, followed by rostral and caudal spreading, supporting the clinical suspicion of PM. Cranial and spinal MRI and blood tests were normal. Clonazepam and levetiracetam achieved PM remission and allowed the withdrawal of sedation. Unfortunately, his general condition worsened and he died due to shock and respiratory failure.
Conclusion: We present the first case of propriospinal myoclonus in the context of SARS-CoV-2 infection. Clonazepam and levetiracetam in combination resulted in resolution of these movements.
Disclosure: There are no conflicts of interest to disclose.

EPR-070

Multiple Sclerosis and Covid-19 Infection: A Single-Centre Experience in Belgium.

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Background and aims: Patients with multiple sclerosis (MS) may be at higher risk of infection and complications from the Coronavirus disease 19 (COVID-19), in part due to the use of disease-modifying treatment (DMTs). The objective of this study was to determine the frequency and severity of COVID-19 in our MS population, and the potential risk factors in contracting this viral infection.
Methods: This is a retrospective single-centre study of all MS patients who attended our neuro-immunology out-patient clinic from May to December 2020. Clinical features, treatments, and outcomes were recorded. COVID-19 infection was identified by means of a positive outcome on PCR testing, serology, or CT imaging.
Results: Of 275 patients studied (mean age 43.4 years, 67.6% women), 28 patients (10.2%) had a confirmed COVID-19 infection. Mean age of this group was 36.4 years, of which 18 (64.3%) were women. 26 had relapsing-remitting MS, one had primary-progressive MS, and one secondary-progressive MS. COVID-19 risk-factors included hypertension (1), a Body Mass Index (BMI) >30 (2) and cancer (1). Six patients were infected during the 1st wave of the epidemic (February-August 2020), in comparison to 22 during the second wave (September-December 2020). Aside from one patient, all were on MS treatment: Teriflunomide (2), Dimethyl fumarate (9), Fingolimod (3), Natalizumab (5), Ocrelizumab (4), Alemtuzumab (1), Cladribine (2), Siponimod (1). One patient needed to be hospitalised. There was no mortality.
Conclusion: Our findings show a good overall outcome for those MS patients infected with COVID-19, with no apparent difference in disease-modifying treatment and COVID-19 disease course.
Disclosure: No disclosure to be made.

EPR-071

Clinical features in patients with COVID-associated parosmia / phanthosmia.

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Background and aims: The purpose of the study is to identify clinical signs in patients with COVID-associated parosmia / phanthosmia.

Methods: The study group consisted of 185 patients 18 years old with COVID-associated parosmia / phanthosmia. SARS-CoV-2 was laboratory confirmed in all patients. The patients were taken from the Telegram group and were interviewed by a doctor after signing an informed consent.

Results: There are 28% of men and 78% of women in the study group. Parosmia was observed in 93% of patients, phanthosmia – 42%, anosmia – 20%, hyposmia – 48%, hyperosmia – 5%. Almost all patients had a history of anosmia (98%). The onset of COVID-associated parosmia is often gradual, while in phanthosmia it is acute. One third of patients had a history of taste disturbance. The comorbid symptoms are increased fatigue – 100%, "head fog" – 55%, sleep disturbances – 46%, recurrent nasal congestion – 25%, burning in the nose – 20%, dryness in the nose – 18%. More than half of the patients have cardiovascular complaints. Most patients have a history of headache, and 69% have migraine. Half of the patients have a history of allergic diseases.

Conclusion: COVID-associated parosmia / phanthosmia is more common in women - gender factor is not excluded. A combination of olfactory disturbances among themselves was more often observed, in almost all parosmia. All patients had persistent comorbid symptoms. Most of the patients had a history of migraine.

Prophylactic anti-migraine therapy can be offered to patients with COVID-associated parosmia / phanthosmia.

Disclosure: Nothing to disclose.

Ageing and dementia 2

EPR-072

Serum Neurofilament light chain levels associate with central nervous system involvement in Pompe

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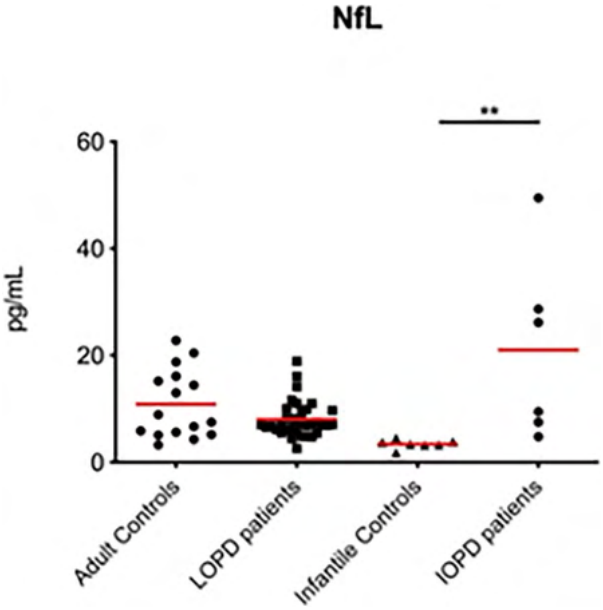
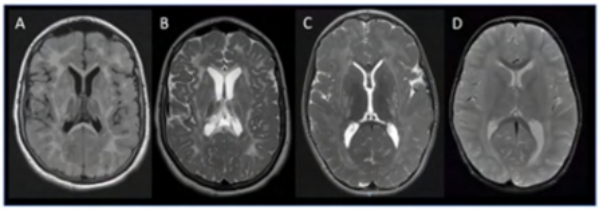
Background and aims: Pompe disease is a rare genetic disorder produced by mutations in the GAA gene with two clear phenotypes described: classic infantile and late onset Pompe disease. Central nervous system involvement is started to be recognized in infantile patients although its prevalence or risk factors are far to be known. To study serum neurofilament light chain levels (sNfL levels) in a cohort of six classic infantile and 35 late onset Pompe patients and compare the results with age matched controls.
Methods: We studied sNfL levels using a commercial kit in the Single Molecule Array (Simoa) platform. Mann-Whitney U test was used to analyze if differences observed were statistically significant. Serum levels were correlated with genetic, clinical and brain MRI data.
Results: sNfL levels were increased in classic infantile Pompe patients compared to controls, while we did not identify significant differences between LOPD patients and controls. Higher sNfL levels were associated with clinical evidence of CNS involvement such as epilepsy, psychomotor delay and spasticity in infantile patients. Brain MRI of patients with symptoms of CNS involvement and higher sNfL levels showed diffuse white matter abnormalities.



NfL serum levels in Pompe patients and controls.



Brain MRI of classic infantile Pompe patients with high serum NfL levels.

Conclusion: Serum NfL levels associate with CNS involvement in classic infantile Pompe patients and may serve as a biomarker to detect brain damage and personalized therapy.
Disclosure: Authors have no relevant disclosures

EPR-073

Parental longevity as a protective factor for Alzheimer's disease

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Background and aims: Despite great effort in identifying risk factors for developing Alzheimer's disease (AD), much remains to be understood. Some studies report an association between longevity of an individual's parents and incidence of AD, but with conflicting results. Furthermore, the role of gender-differential in parents' longevity and dementia remains particularly unexplored. Our aim was to investigate whether later age of parents' death may act as a protective factor for AD.
Methods: Case-control study performed at Coimbra Hospital and University Centre. Cases were defined as adult patients with diagnosis of AD according to current criteria. Controls were defined as adults with normal cognitive performance, and no neuropsychiatric disorder. A structured questionnaire was applied to all subjects. Multivariate analysis was conducted with logistic regression, to identify independent variables associated with status (control vs. cases).
Results: We included 225 subjects, 111 AD patients and 114 controls. Groups were comparable for level of education. We found mothers' age of death to be significantly higher in control vs. AD group (81.6±12.3 vs. 77.2±13.7, p=0.015). No difference was found between fathers' age of death (75.0±13.8 vs. 74.0±15.4, p=0.552). These findings remained after excluding patients and controls with a positive family history for dementia. On logistic regression, maternal age of death (OR=0.969, 95%CI= [0.947, 0.992], p=0.008) remains statistically significant.
Conclusion: Later maternal age of death appears to act as a protective factor for AD. This gender-differential in parents' longevity provides further insight on a maternally inherited pathophysiology in AD, deserving further investigation.
Disclosure: Nothing to disclose.

EPR-074

Phosphorylated neurofilament heavy chain in MNDs with UMN symptoms: candidate biomarkers for diagnosis and prognosis

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Background and aims: The diagnosis and prognosis of patients presenting with upper motor neuron symptoms may diverge from amyotrophic lateral sclerosis (ALS) (classic and UMNp-ALS), to primary lateral sclerosis (PLS) and hereditary spastic paraparesis (HSP). Differential diagnosis among these syndromes characterized by distinct prognosis still relies on long-term follow-up. Neurofilaments have emerged as biomarkers of neurodegeneration in many neurological diseases [1] and have shown to be potential diagnostic and prognostic biomarkers for ALS [2–3] . The objective of this study was to test whether phosphorylated neurofilament heavy chain (pNfH) may discriminate different UMN syndromes at diagnosis and to test their prognostic role.
Methods: We measured CSF and serum pNfH of 141 patients presenting with UMN signs and diagnosed with ALS, UMNp-ALS, hSP, and PLS.
Results: ALS and UMNp-ALS patients had higher levels of CSF and serum pNfH compared to PLS and hSP. PLS and hSP patients had similar CSF and serum pNfH concentrations. ROC curves for discriminating ALS (including UMNp-ALS) from PLS – hSP showed an area under the curve of 0.76 for CSF and 0.72 for serum. In multivariable survival analysis including relevant clinical factors, CSF pNfH represented one of the strongest variables predicting survival.
Conclusion: This study supports the role of CSF pNfH as prognostic biomarkers of MND presenting with UMN signs. A potential discriminative power between ALS/UMNp-ALS and other UMN syndromes with favourable prognosis (PLS/hSP) at presentation has been detected both for CSF and serum pNfH.
Disclosure: Nothing to disclose.

EPR-075

Alzheimer's disease risk loci are not associated with the rate of cognitive decline in older adults with type 2 diabetes

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Background and aims: Type 2 diabetes (T2D) is an important risk factor for cognitive decline and dementia. In the last decade, multiple risk loci for late-onset Alzheimer's disease (LOAD) were discovered.
Methods: We studied the association of LOAD loci with cognitive decline in the Israel Diabetes and Cognitive Decline (IDCD) cohort, of initially cognitively normal Jewish elderly with T2D (>65 years old), who were followed up every 18 months for a period of 54 months. Mixed regression models, assuming an additive genetic model and adjusting for age, sex, education and ancestry (Ashkenazi/non Ashkenazi) examined the associations of each of the genes with global cognitive decline.
Results: 22 SNPs and the APOE E4 allele were examined in 944 participants (average age at baseline: 72.5 years). None of the variants was associated with change in global cognitive functioning, after correction for multiple testing. Results were similar for associations with specific cognitive domains of episodic memory, attention/working memory, executive functions and language or when adjusting also for diabetes-related and cardiovascular risk factors.
Conclusion: Taken together, our results do not support contribution of LOAD loci to cognitive decline in elderly with T2D.
Disclosure: Nothing to disclose.

EPR-076

Hospital readmissions following infections in dementia, a nationwide and registry-based cohort study

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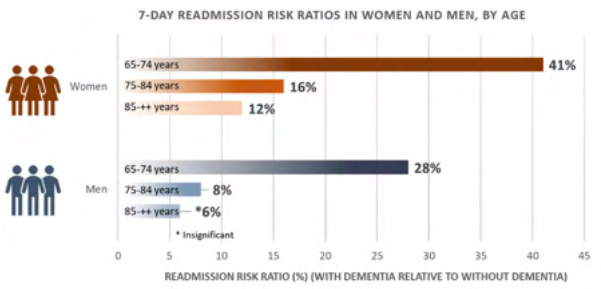
Background and aims: Readmissions put persons with dementia at risk for adverse health outcomes. Relatively little is described in literature about their hospitalization trajectories after admissions for infections. We aimed to investigate readmission risks (with dementia and without); identify types of infections behind risks; and highlight reasons for readmissions.
Methods: Registry-based cohort of elderly patients with acute inpatient hospital admissions for infections in Denmark included from January 1, 2000 or age 65 years. Primary outcomes: 7-day readmissions (Risk Ratios [RR]: Risk following index admissions with dementia relative to without); risks by infection site, and reasons for readmission (secondary: 30- and 90-day readmission). Competing risk of death was estimated.
Results: 789,732 index admissions (421,133 people) were included and resulted in 55,303 7-day readmissions and 78,732 deaths. Readmission and mortality RRs were higher following index admissions for infections than for other causes. 7-day readmission RR was increased in all ages and highest in the youngest (Women RR 1.41, 95% confidence interval [CI] 1.26–1.58; Men RR 1.28, 95% CI: 1.16–1.40). RRs decreased with increasing age and longer follow up. Readmission risks were higher following admissions with dementia in the youngest ages in all infection sites, and reasons for readmission were commonly due to infection (linked/unresolved or other infection) and dehydration.



Conclusion: Findings highlight need for improvements in preventing and treating infections in people with dementia, and in ensuring successful transition from the hospital to the community. In-depth investigations of factors related to readmissions are needed, to highlight important avenues for interventions to decrease or prevent potentially avoidable readmissions.
Disclosure: Nothing to disclose.

EPR-077

Factors influencing serum neurofilament light chain levels in normal ageing

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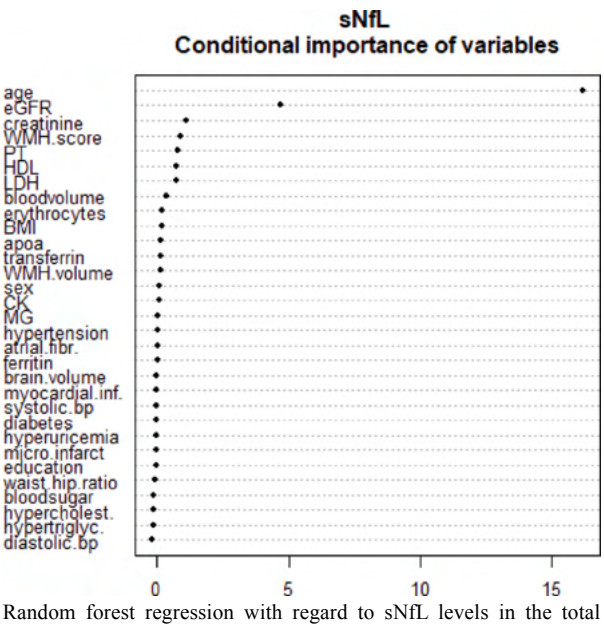
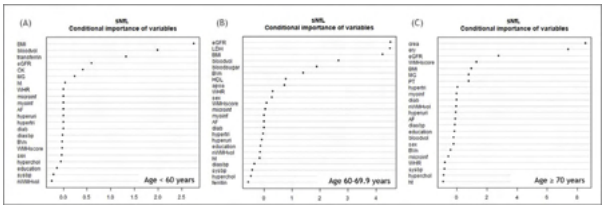
Background and aims: Serum neurofilament light (sNfL) is a promising marker for neuro-axonal damage and it is now well known that its levels also increase with higher age. However, the effect of other potential factors than age is still poorly investigated. We therefore aimed to identify factors influencing sNfL concentrations by analysing a large set of demographic, laboratory and imaging variables in a normal ageing cohort.

Methods: sNfL was quantified by a single molecule array (Simoa) in 292 (mean age 64.8±10.6 years, 176 female) neurologically unconspicuous individuals who participated in the Austrian Stroke Prevention Family Study (ASPSF). Random forest regression analysis was used to rank the importance of included variables on sNfL. Backward linear regression and Area under the Receiver-Operating-Characteristics (AUC-ROC) then served to identify factors independently influencing sNfL levels.

Results: Age was by far the most important factor influencing sNfL (figure 1), which was mainly driven by individuals >60 years. In age stratified sub-groups (figure 2), body mass index (BMI) independently predicted sNfL in individuals aged 38–60 years (beta=-0.258, p=0.030, AUC=0.885). In the age-group 60–69.9 years, BMI (beta= -0.237, p=0.015, AUC=0.791) was accompanied by estimated glomerular filtration rate (eGFR, (beta=-0.241, p=0.017, AUC=0.813) and lactate dehydrogenase (LDH) (beta=0.228, p=0.023, AUC=0.759), whereas in individuals >70 years creatinine (beta=0.296, p=0.001, AUC=0.692) and erythrocyte count (beta=-0.274, p=0.002, AUC=0.649) predicted sNfL.



Random forest regression with regard to sNfL levels in the total sample.



Random forest regression with regard to sNfL levels in age groups.

Conclusion: Age is the most important factor influencing sNfL concentrations, which gets increasingly relevant in elderly people. BMI further influences sNfL levels, especially at younger age, whereas kidney function may be additionally relevant in the elderly.

Disclosure: Authors have nothing to disclose.

EPR-078

Frontotemporal lobar degeneration phenotypes misdiagnosed with Alzheimer's disease.

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Background and aims: Frontotemporal lobar degeneration (FTLD) are neurodegenerative diseases, with heterogeneous clinical disorders, including changes in behaviour, language, executive function and motor skills. These symptoms could also be observed in Alzheimer's disease (AD) which may result in diagnostic errors. This study sought to characterize which phenotypes of FTLD are difficult to distinguish from AD.
Methods: Among the patients followed in the Lille and Bailleul Memory Clinic (France) between 1993 and 2019 and having a formal diagnosis of FTLD (through histological confirmation or FTLD autosomal dominant mutation presence), the clinical phenotypes of those for whom there was a diagnostic doubt between FTLD and AD ("hesitation group", n=30) were compared with the clinical phenotypes of those there for whom there was no doubt in diagnosing FTLD ("no hesitation group", n=46).
Results: A progressive supranuclear palsy syndrome (PSP-S) phenotype and a frontotemporal dementia with motor neuron disease (FTD-MND) phenotype are only found in the "no hesitation group" (PSP-S n=5/46, 10.9% ; FTD-MND n=6/46, 13.0%). A typical behavioural variant of frontotemporal dementia (bvFTD) phenotype is observed in both groups ("hesitation group" n=14/30, 46.7% ; "no hesitation group" n=24/46, 52.2%). A memory and behavioural phenotype (but not fulfilling Rascovsky criteria for possible bvFTD) is only found in "hesitation group" (n=5/30, 16.7%).
Conclusion: Despite typical clinical presentation, some bvFTD patients may lead to diagnostic issues. On the other side, Rascovsky criteria sometimes fail to diagnose FTLD in a few cases of patients with a memory and behavioural phenotype.
Disclosure: There is no actual or potential conflict of interest in relation to this study.

EPR-079

Physiotherapy with dual-tasks improves cognition in Parkinson's disease with postural instability and gait disorders

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Background and aims: To assess cognitive changes following a 6-week training associated with dual-task gait/balance exercises in PD patients with postural instability and gait disorders (PD-PIGD).
Methods: 25 PD-PIGD patients were randomized into two groups: i) action observation training (AOT) and motor imagery (MI)+DUAL-TASK group performed a 6-week (W6) training consisting of AOT-MI combined with practicing observed-imagined gait and balance exercises; ii) DUAL-TASK-group performed the same exercises combined with landscape-videos observation. At baseline, W6 and W14 patients underwent neurological, computerized cognitive and motor evaluations. A group of 23 healthy controls (HC) underwent a neuropsychological assessment at the study entry only. Cognitive changes in patients were monitored with the CANTAB (Cambridge Neuropsychological Test Automated Battery). Cognitive changes at each time point in the overall PD-PIGD sample and between groups (AOT-MI + DUAL-TASK and DUAL-TASK) were assessed.
Results: At baseline, no cognitive differences were found between the two PD-PIGD groups. However, both PD groups performed worse than HC in several cognitive domains. Over time, both PD groups improved in terms of gait velocity and balance. Regarding cognitive changes, at W6 and at W14, all PD patients improved in terms of accuracy and reaction times in tests assessing attention switching and visuospatial localization abilities. No differences were observed between groups over time.
Conclusion: A physiotherapy approach associated with dual-task gait/balance exercises can improve cognitive performances in PD-PIGD patients that persist at long term. This improvement is evident in specific cognitive domains, which are usually affected in PD-PIGD and can interfere with their motor performances.
Disclosure: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Cerebrovascular diseases 2

EPR-080

Association of chronic Covert Brain Infarction with Etiology of First-Ever Acute Ischemic Stroke

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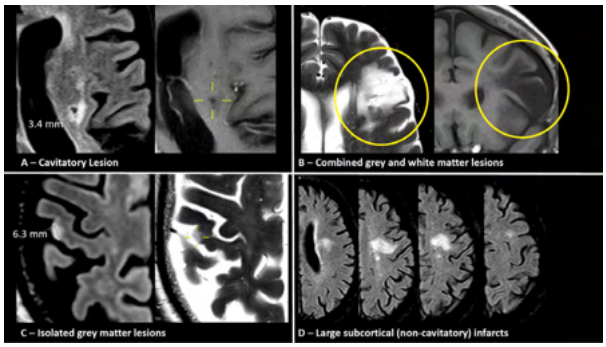
Background and aims: Chronic covert brain infarction (CBI) are frequent incidental findings in patients with acute ischemic stroke (AIS), but their usefulness to determine the etiology of the acute ischemic event remains uncertain.
Methods: Cohort study including patients from 2015 – 2017 with blinded observers. Single, academic stroke center using MRI as the primary admission imaging modality. Consecutive sample of patients with first ever AIS.



Phenotypes of covert brain infarction

Results: 574/1543 patients (37%) had a total of 950 chronic CBIs. 314 (20.4%) had at least one cavitatory CBI, and 192 (12.4%) at least one CBI with cortical involvement. 1543 patients (median [IQR] age, 71 [60–81] years; 40% women, NIHSS 3 [1–8]) were included. Whereas 42% of patients with large-artery atherosclerosis, 41% with small-vessel occlusion and 41% of patients with cardioembolism had at least one CBI, CBI presence was infrequent in cervical artery dissection (8%) and persistent foramen ovale (19%, $p<0.001$). The presence of any cortical CBI was associated with cardioembolism (aRRR 3.1, 95% CI 1.2–8.3) and large-artery atherosclerosis (aRRR 3.8, 95% CI 1.4–10.5) as compared to small-vessel disease. There was no clear association of the presence of neither an additional CBI within the same vascular territory nor CBI presence within a different vascular territory as the AIS with AIS etiology.
Conclusion: CBI presence and phenotypes are associated with certain stroke subtypes in patients with first-ever acute ischemic stroke. Additional studies need to clarify whether CBI could refine individualized diagnostic work-up and therapeutic approaches.
Disclosure: Nothing to disclose.

EPR-081

A paramedic survey on prehospital stroke care, training needs, and current attitude toward lithuanian stroke network

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[1] Faculty of Medicine, Vilnius, Lithuania, [2] Department of Neurology, Vilnius, Lithuania, [3] Department of Neurology, Boston, United States

Background and aims: Emergency medical services are the first healthcare contact for the majority of stroke patients. Currently, there is no data evaluating Lithuanian paramedics' stroke-related knowledge.

Methods: We surveyed Vilnius paramedics from September to November 2019. Paper questionnaire included questions on prehospital stroke care, stroke training needs, and attitudes toward Lithuanian stroke network. We compared the answers between city and district paramedics.

Results: Out of 161 surveyed paramedics, 97 (60.2%) worked in Vilnius city, 59 (36.6%) in the district, and five (3.1%) worked in both. Their mean age was 49.9±10.0 years, 74.5% were female, 72.0% had >20 years of work experience. Fewer district than city paramedics rated their prehospital stroke care knowledge as sufficient (52.4% vs. 69.3%, p=0.040), and 81.3% vs. 69.3% (p=0.038) indicated a need for additional stroke training. Respondents reported being confident or highly confident while dealing with stroke (71.3%), polytrauma (60.0%), myocardial infarction (48.1%), and sepsis (35.8%) (p<0.001). Vertigo (60.8%), brain tumours (56.3%), and seizures (54.4%) were indicated as the most common stroke mimics. Only 6.2% of respondents received formal feedback on suspected stroke patients brought to the emergency department. The current Lithuanian stroke network was evaluated positively or very positively by 85.2% of respondents.

Conclusion: Vilnius district paramedics rate their prehospital stroke care knowledge significantly worse than those working in the city, and there is a need for further stroke training in both groups. The feedback to paramedics on suspected stroke patients is insufficient, nevertheless, paramedics maintain a positive attitude toward the current stroke network practice in Lithuania.

Disclosure: We have nothing to disclose.

EPR-082

24h ambulatory blood pressure monitoring predicts progression of cerebral small vessel disease

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Background and aims: Cerebral small vessel disease (CSVD) is one of the most important and common vascular disorders of the brain caused by lacunar infarcts or white matter lesions (WMLs). Predictors of its radiological progression are not well known. We aimed to evaluate the influence of baseline 24h ambulatory blood pressure (BP) profile on the long-term risk of radiological CSVD progression.

Methods: We recruited patients with CSVD who underwent the 24-h ambulatory blood pressure monitoring and the brain MRI scans at baseline and after two years follow-up. Mean 24-hour arterial blood pressure (MAP), daytime and nighttime average systolic BP (meanSBP), diastolic BP (meanDBP) were recorded. Nocturnal dipping was also analyzed.

Results: 123 patients with an average age of 72.4 years were enrolled in our study. Above one-third of patients (34,9%) experienced radiological progression during the study flow. There were no significant baseline clinical or radiological differences between patients without progression (Group 1) and who progressed (Group 2) (Table 1). MAP, daytime meanSBP and meanDBP were significantly higher in the lacunes progression group than those in the no-progression group (Table 2). There were no significant differences in these measurements between WMLs progression group and no-progression group. There was no significant difference in precentage of non-dipper pattern between groups.

variables	No progression Group 1	Radiological progression Group 2	p
N	80	43	-
SVD manifestation; N (%)			0,09
LS	37 (46,3)	12 (27,9)	
VaD	26 (32,5)	22 (51,2)	
VaP	17 (21,3)	9 (20,9)	
Age, mean (±SD) years	71,4 (8)	73,4 (8,1)	0,21
Female sex	41 (51,3)	19 (44,2)	0,57
Hypertension	69 (86,3)	37 (86)	0,99
Coronary artery disease	18 (22,5)	6 (14)	0,34
Diabetes mellitus	46 (56,3)	23 (53,5)	0,85
Current smoking	25 (31,3)	12 (27,9)	0,83
Hyperlipidemia	62 (77,5)	29 (67,4)	0,28
Peripheral arterial disease	5 (6,3)	5 (11,6)	0,31
Polymetabolic Syndrome	37 (46,3)	16 (37,2)	0,34
Obesity (BMI>30 kg/m^2)	63 (78,8)	29 (67,4)	0,19
CKD	9 (11,3)	9 (20,9)	0,18
Antihypertensive treatment n(%)	(90.4)	(88.3)	0.44
Fazekas Score (mean)	2 (0,76)	2,23 (0,53)	0,09
Fazekas PVH	1,53 (0,98)	1,62 (0,85)	0,71
Fazekas WMH	1,47 (0,87)	2,04 (0,87)	<0,01
SVD score (mean)			0,40
0	2 (2,5)	0	
1	23 (28,8)	12 (27,9)	
2	22 (27,5)	18 (41,9)	
3	20 (25)	9 (20,9)	
4	13 (16,3)	4 (9,3)	
Lacunes	42 (52,5)	18 (41,9)	0,34
Microbleeds	14 (17,5)	5 (11,6)	0,44
PVS	34 (42,5)	19 (44,2)	0,99
Atrophy	20 (25,3)	13 (30,2)	0,67

Values are means (±SD) or numbers of patients (%)
Continuous variables were compared using the Mann-Whitney U test. The Chi-square test was used for frequency comparisons
SVD – small vessel disease, VaD – vascular dementia, VaP – vascular parkinsonism; LS – lacunar stroke; BMI – body mass index; BI – Barthel Index; CKD chronic kidney disease; IS – ischemic stroke; MI – myocardial infarction

Baseline clinical and radiological characteristics of studied patients with cerebral small vessel disease without radiological progression (Group 1) and with progression (Group 2).

	WMLs+lacunes			Lacunes			WMLs		
	1-No progression	2- progression	p	1-No progression	2- progression	p	1-No progression	2- progression	p
MAP, mmHg	93,11 ± 11,76	97,38 ± 12,66	,151	92,68 ± 11,58	100,91 ± 12,62	,020	94,01 ± 12,32	95,74 ± 11,67	,598
SBP, mmHg	132,45 ± 16,91	135,29 ± 16,79	,494	131,64 ± 16,68	140,47 ± 15,99	,067	133,64 ± 17,28	132,22 ± 15,55	,756
DBP, mmHg	73,44 ± 10,96	78,42 ± 11,65	,072	73,50 ± 10,74	81,13 ± 12,09	,018	74,20 ± 11,45	77,50 ± 10,87	,280
Daytime									
MAP, mmHg	92,97 ± 10,77	97,42 ± 13,54	,133	92,66 ± 11,31	101,67 ± 11,34	,009	93,82 ± 10,99	96,12 ± 14,37	,482
SBP, mmHg	132,19 ± 15,57	134,78 ± 17,33	,523	131,21 ± 16,27	140,71 ± 12,89	,045	133,03 ± 15,28	132,82 ± 18,98	,962
DBP, mmHg	73,37 ± 10,01	78,74 ± 12,73	,053	73,38 ± 10,35	82,14 ± 11,86	,007	74,21 ± 10,49	77,76 ± 12,97	,248
Nighttime									
MAP, mmHg	88,76 ± 13,86	92,91 ± 17,36	,280	88,71 ± 14,24	96,03 ± 17,44	,111	89,65 ± 14,86	91,25 ± 15,85	,708
SBP, mmHg	127,63 ± 20,15	130,27 ± 23,60	,626	126,98 ± 19,90	135,15 ± 25,88	,207	129,02 ± 21,76	126,25 ± 19,00	,646
DBP, mmHg	69,33 ± 12,83	74,23 ± 15,84	,166	69,57 ± 13,38	76,46 ± 15,26	,104	69,97 ± 13,33	73,75 ± 15,77	,337
Non dipper pattern (%)	43,60%	36%	0,52	43,90%	28,60%	0,28	0,41%	0,42%	0,9

Values are means (±SD) or numbers of patients (%).
Nocturnal dipping was defined as a reduction in average SBP and DBP at night greater than 10% compared with average daytime values.

24h-ABPM measures of studied patients with cerebral small vessel disease without (Group 1) and with radiological progression (Group 2) divided by the radiological group.

Conclusion: ABPM may help assess the risk of new lacunes but not the WMLs progression, mainly by measuring 24h MAP, daytime meanSBP and meanDBP. Nighttime BP control seems to play a minor role. The dipper / non dipper profile is also irrelevant.
Disclosure: No conflict of interest

EPR-083

Development of a patient decision aid regarding discharge planning for hospitalised patients with stroke

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Background and aims: Individual stroke care could be improved by promoting shared decision-making (SDM) supported by outcome information. Therefore, a patient decision aid (PtDA) was developed focusing on discharge planning of patients with stroke.
Methods: A convergent mixed methods design was used, starting with quantitative surveys among patients (n=52) and health care professionals (n=86), followed by three focus groups with patients. This data was used to develop the PtDA in five co-creation sessions with stakeholders. Usability testing of the tool was conducted with patients (n=7) and health care professionals (n=35) to further optimise the PtDA. Development was guided by the International Patient Decision Aids Standards criteria.
Results: Patients and health care professionals indicated that the (outcome) information in the PtDA should be brief but complete and displayed clearly. A 3-step PtDA was developed, each supporting a step in the SDM process: 1) a printed consultation sheet to introduce the decision, containing basic information that can be specified for each individual patient; 2) an online information and deliberation tool to support patient education and values clarification, containing a integrated "patients like me" model about discharge locations; 3) a summary sheet to support actual decision-making during consultation, containing patients' values and preferences concerning discharge planning. The usability test revealed that patients and health care professionals highly appreciated the PtDA with integrated outcome information.
Conclusion: The developed PtDA was found acceptable for patients and health care professionals and is currently under investigation in a clinical trial to determine its effectiveness.
Disclosure: No conflicts of interest

EPR-084

Simultaneous cavernous sinus thrombosis and carotiditis with acute ischemic stroke as a complication of sinusitis

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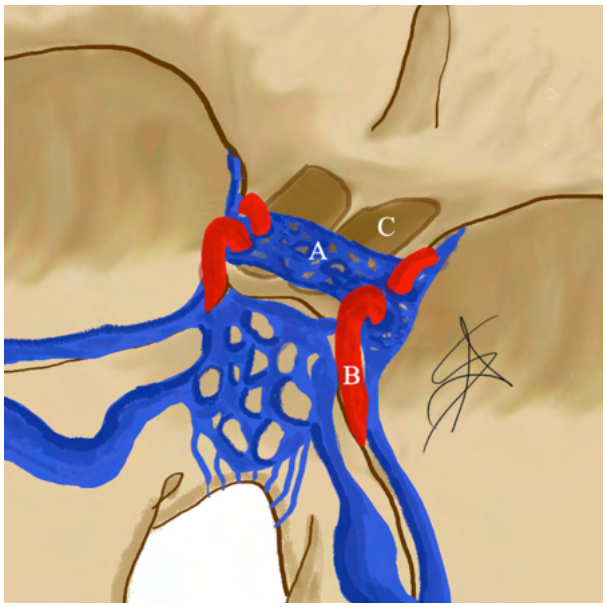
Background and aims: Acute sinusitis is a common affection of the upper airways usually characterized by a good prognosis if correctly managed. Dissemination of infection by contiguity represents the most common complication and neurological complications are rare. We describe our single center experience and propose a literature review.



Anatomical view: A. Cavernous sinus; B. Internal carotid artery; C. Sphenoidal sinus

Methods: This retrospective study was conducted on patients admitted at Lausanne University Hospital between 2005–2020 with a diagnosis of bacterial sinusitis complicated by cavernous sinus thrombosis and concomitant acute ischemic stroke from carotiditis. CARE guidelines were adopted. We provided description of patient characteristics, clinical data, treatment and functional outcome. We then integrated our cases with those reported in literature using appropriate search terms in Medline.
Results: We identified three patients from our case series and one from literature who presented such neurovascular complication. Median age was 31 (range 15–60). All patients had a middle cerebral artery stroke with 16.5 as median onset NIHSS (range 2–26). Neurological complication occurred at median seven days from acute sinusitis (3 sphenoidal, one spheno-ethmoidal; two S. Aureus, one F. Necrophorum, one undetermined). All patients received endoscopic sinus drainage and broad-spectrum antibiotics; three patients received anticoagulation, one antiplatelet treatment. At 3-months, two patients had a good functional outcome (mRS2), one was not independent (mRS=4) and one was declared palliative and died.

	Patient 1	Patient 2	Patient 3	*Patient from literature* (Bentham et al, 2004)
Patient and lesion characteristics				
Age	24	38	64	15
Sex	Male	Male	Female	Female
Sinusitis location	Bilateral sphenoidal	Bilateral sphenoidal and ethmoidal	Left sphenoidal	Bilateral sphenoidal
Venous thrombosis	Left CS, Bilateral IJV	Bilateral CS, right IJV, left SS, right SOV	Left CS	Right CS
Carotiditis	Bilateral ICA	RIght ICA	Left ICA	Right ICA
Stroke location	Deep bilateral MCA territory	Deep right MCA territory	Cortical left MCA territory at onset, deep left MCA on vasospasm	Deep right MCA territory
Sinusitis-to-neurological complication	11 days	3 days	0 days	14 days
Microbiology				
Germ sinusitis	S. aureus	S. aureus	Undetermined	S. epidermidis
Germ bacteraemia	S. milleri	S. Aureus	No bacteraemia	F. necrophorum
Interventions				
ORL intervention	Bilateral sphenoidectomy, left paracentesis	Bilateral sphenoidectomy	Left sphenoidectomy	Bilateral sphenoidectomy, left ethmoidectomy
Broad-spectrum antibiotics	Yes	Yes	Yes	Yes
Acute anticoagulation	Yes	Yes	Yes	No
Acute antiplatelets	No	No	No	Yes
Long term antithrombotic	Clopidogrel	Aspirin	No	Aspirin discontinued (gastrointestinal bleeding)
Outcome				
3-month mRS	1	2	6	4
Delta pre-mRS -> mRS	1	2	4	4
12-month mortality	No	No	Yes	n/a

ICA= Internal carotid artery; MCA= Middle cerebral artery; IJV= Internal jugular vein; CS= Cavernous sinus; SS= Sigmoid sinus; SOV= Superior ophthalmic vein; pre-mRS= pre-stroke modified Rankin score; mRS= modified Rankin score

Summary of patients

Conclusion: Simultaneous cavernous sinus thrombosis and carotiditis with acute ischemic stroke is a rare complication of bacterial sinusitis that should be considered. It may have a good outcome if promptly and appropriately treated by endoscopic sinus drainage, broad-spectrum antibiotics and antithrombotics.
Disclosure: Nothing to disclose.

EPR-085

Rete middle cerebral artery aneurysm: a case-based update

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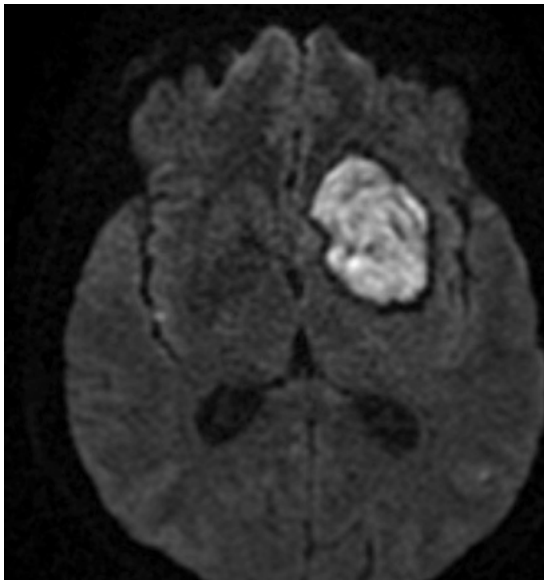
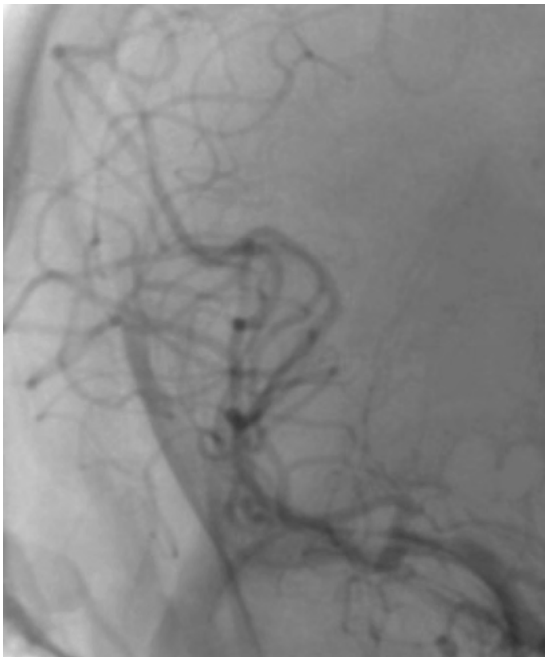
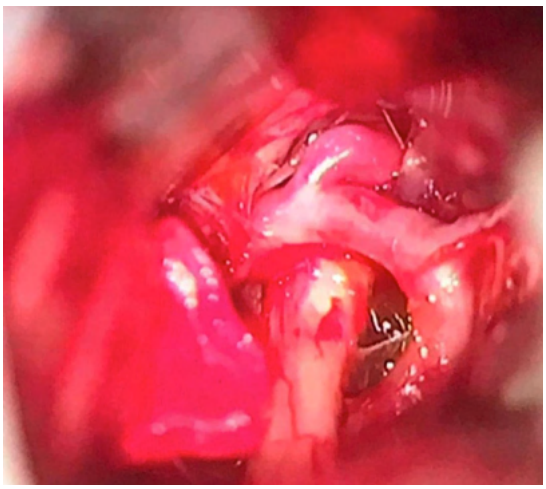
Background and aims: A rete middle cerebral artery (MCA) is an extremely rare and poorly discussed MCA anomaly. It is a weblike abnormality of the MCA which does not coalesce and forms a prominent single branch from the plexiform vessels in the fetal stage, being associated with aneurysms.
Methods: Retrospective chart review of clinical data and imaging of a patient who presented with ruptured aneurysm in a rete MCA. A discussion and literature review of the condition are presented.
Results: A 50-year-old woman presented with severe headache, altered consciousness, aphasia, and right hemiplegia. CT, MRA, and DSA revealed a frontal hematoma and two left MCAs. Intraoperatively, the accessory MCA presented the largest caliber and had an extensive network of plexiform branches (rete MCA). The M2 segments were dissected and the hematoma was evacuated. In a MCA branch close to the hematoma, it was identified and clipped an aneurysm (7-mm right clip).



Preoperative imaging: axial FLAIR MRI demonstrating a left frontal intraparenchymal hematoma.



Preoperative imaging: DSA demonstrating a web-like abnormality of the left MCA (rete MCA).



Intraoperative imaging: view of the aneurysm in a MCA branch.

Conclusion: To date, 13 cases of rete MCA aneurysm were reported in literature. Clinical manifestations include altered consciousness (~83%), headache (~42%), hemiparesis (~33%), facial paralysis (~17%), and nausea/vomiting (~8%). The rete MCA presents a thinner muscular layer, being more vulnerable to hemodynamic stress and aneurysm formation. In case of suspicion in CT/MRA, DSA must be realized to identify rete MCA features and aneurysm location, size, and shape. Aneurysm clipping or trapping appears to be a good therapeutic option. Although rare, it is important to be aware of the possible aneurysm formation in this MCA anomaly to prevent misdiagnosis and adverse outcomes.
Disclosure: The authors report no conflict of interest.

EPR-086

Evaluation of blood pressure control post-stroke in a cohort of ischemic stroke patients

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Background and aims: There is limited data regarding BP control after stroke in European countries with reports indicating values around 37% of BP control in follow-up appointments Our objective was to evaluate the proportion of stroke patients with controlled BP at 3- and 12-months post stroke and to determine predictors of lack of BP control in a cohort of patients.
Methods: Prospective cohort study of patients admitted with a diagnosis of ischemic stroke to an university hospital from January 2017 to May 2020. Patients were prescribed anti-hypertensives on hospital discharge if applicable. BP was assessed 3- and 12-months post-stroke, according to a protocol (3 repeated measurements and determination of mean). Controlled BP was defined as SBP<140 and DBP<90mmHg (SBP<130 and DBP<80mmHg in diabetic patients <65years old). The proportion of patients with BP controlled at 3- and 12-months post-stroke was determined. Variables associated to BP control on follow-up were determined.
Results: 698 patients (42,4% female) were included, mean age of 68 years old. 3- and 12-month post-stroke BP control rate was 51,8% and 51,6%, respectively. Only 32% of patients had controlled BP in both assessments. Younger age was associated with a better control of BP. A prior diagnosis of hypertension or diabetes mellitus was significantly associated with having uncontrolled BP in follow-up appointments (p<=0,001).
Conclusion: The percentage of patients with controlled BP was higher than previously reported, but it is still not ideal. Knowing which variables are predictors of lack of BP control on follow-up may help to design targeted strategies.
Disclosure: This work received funding from "23º Programa 'Educação pela Ciência' | Bolsas CHULN".

EPR-087

Platelet aggregometry in stroke prevention after carotid stenting: a prospective cohort in a tertiary hospital.

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Background and aims: Dual Antiplatelet Therapy after carotid artery stenting is considered the gold standard treatment. However, the antiplatelet therapy response could be different among patients, and a posology adjustment could be required. Platelet aggregometry is a useful tool to objectively measure this response in vitro. We aim to evaluate the clinical usefulness of this technique in order to handle antiplatelet therapy posology and evaluate if the aggregometry-adjusted posology is related to early restenosis and stroke recurrence.
Methods: A prospective cohort study is proposed. We collected all carotid stentings performed between 2013 and 2019. As inclusion criteria, all patients were treated with dual antiplatelet therapy consisting in Aspirin 100mg and Clopidogrel 75mg since at least one week before the procedure. An aggregometry test using Verify® was performed just before the procedure. Two groups depending on the aggregometry-adjustment posology made by the neurologist were done. Follow-up imaging and clinical outcome were observed.
Results: 97 patients were collected. Among them, 52 (53.6%) of them were low-responders (38 to Clopidogrel, 23 to Aspirin, nine to both). In 17 (32.7%) patients among those low-responders ones, an aggregometry-adjusted posology was performed, and in 35 (67.3%) patients was not. No statistically significative differences in restenosis at 24hours (p=0,944), at three months (p=0,792) and after one year (p=0,421) were detected; neither in stroke recurrences after one year (p=0,603).
Conclusion: The aggregometry-adjusted posology in dual antiplatelet therapy was not associated to a better clinical neither ecographical evolution. More studies are needed to determine the place of platelet aggregometry.
Disclosure: Nothing to disclose.

Epilepsy 2

EPR-088

An updated safety review of eslicarbazepine acetate in pregnancy after 11 years of post-marketing experience

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Background and aims: Epilepsy management during pregnancy may be challenging, especially in those taking antiseizure medications (ASMs), when balancing the risk of potential adverse effects of ASMs on the foetus with the risk of uncontrolled seizures in the mother. We aim to report an update of safety data on pregnancy and foetal/postnatal outcomes following 11 years post-marketing surveillance experience (PMS) with eslicarbazepine acetate (ESL).
Methods: Pregnancy cases with exposure to ESL were retrieved from the global safety database from April 21st, 2009 until November 30th, 2020. The Embase™ and MEDLINE® databases were also searched to identify additional literature reports on use of ESL during pregnancy.
Results: A total of 3986 ESL safety reports were received [753 from clinical trials (CTs) and 3233 from post-marketing surveillance (PMS)], of which 185 corresponded to pregnancy related notifications. From the latter, 176 reports referred to ESL exposure: 29 reported in CTs and 147 in PMS. In 59 pregnancy cases the outcome was unknown or ongoing, while 72 cases resulted in live birth without anomalies. From 28 abortions reported, 13 corresponded to induced abortions and 15 to spontaneous events. Nine congenital anomalies were identified, but no clear relationship with ESL exposure was established. The literature search did not provide additional cases.
Conclusion: No new relevant safety concerns were identified from 11 years PMS data analysis of pregnant women exposed to ESL. As the impact of ASMs requires long term assessment, ESL exposure during pregnancy will continue to be monitored and analysed, to further characterize ESL safety profile.
Disclosure: Work supported by BIAL- Portela & Ca, S.A., S. Mamede do Coronado, Portugal

EPR-089

Correlates of psychological distress in epileptic patients during the COVID-19 outbreak

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Background and aims: In late 2019, a novel coronavirus termed SARS-CoV-2 was isolated from human cases. To date no studies have analyzed the role played by the different dimensions of psychological distress quarantine induced in patients with epilepsy.
Methods: We included a total of 40 patients, 18 suffered from generalized, and 22 from focal epilepsy. The patients previously seen in the outpatient clinic during the pre-lockdown period between January and February 2020 were re-evaluated after the lockdown period of March and April 2020. Psychological distress was evaluated by using the three subscales of Impact of Event Scale-Revised (IES-R) tapping intrusion, avoidance and hyperarousal related to traumatic event.
Results: As for the overall sample, the number of epileptic attacks was significantly higher at post-lockdown than at pre-lockdown. The same pattern of results was observed for patients with high scores on IES-R Intrusion and IES-R Avoidance subscales. Multivariate logistic regression analyses showed that: 1) higher scores on IES-R Intrusion subscale were associated with higher age, female sex, and higher scores on HADS-Anxiety subscale; 2) higher scores on IES-R Hyperarousal subscales were related to higher scores on HADS-Anxiety subscale; 3) higher scores on IES-R Avoidance scale were associated with higher age, and higher scores on HADS-Anxiety subscale.
Conclusion: The frequency of epileptic seizures increased during lockdown (months March and April) when compared to pre-lockdown period (months January and February). This pattern of increased frequency is particularly notable for older female patients which experienced with higher intrusivity and avoidance and suffered from more marked anxious symptoms.
Disclosure: Nothing to disclose.

EPR-090

Predictors of long-term outcome in mesial temporal lobe epilepsy patients after selective amygdalohippocampectomy

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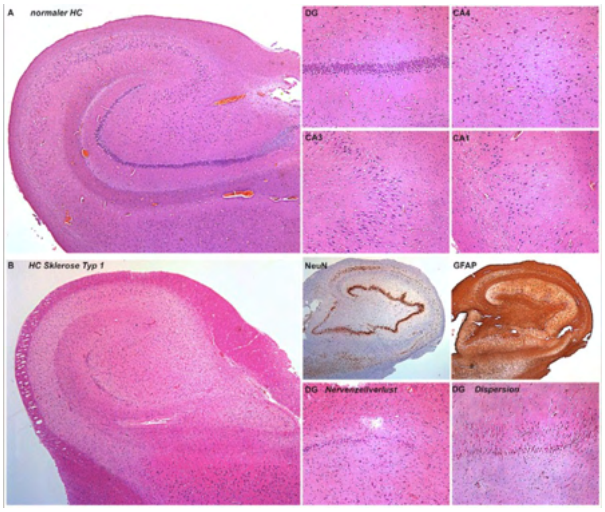
Background and aims: Surgical treatment of patients with mesial temporal lobe epilepsy (MTLE) with hippocampal sclerosis (HS) evolved to an effective treatment option, but postoperative clinical course is variable. The aim of the study was to evaluate the impact of different clinical variables for possible prognostic implications on postoperative seizure and cognitive outcome in patients with MTLE.

Methods: 150 patients (74 females, mean age 37.4 y., mean age at epilepsy onset 12.2 y., mean age at surgery 37.4 y.) with drug-resistant MTLE who underwent SAHE at the Vienna Epilepsy Surgery Program of the Medical University of Vienna, Austria between 1994 and 2017 were included. Resected tissue was reclassified according to new ILAE classification. We performed backwards stepwise regression analysis to investigate which of the explanatory parameters can predict the outcome best.

Results: At the last available follow-up visit 11.1±5.9 years after surgery 102 patients (69.4%) were seizure-free (Class 1a+1). History of traumatic brain injury at one year after surgery, and female sex and higher number of preoperative AEDs at years two and five after surgery were significantly associated with worse postoperative outcome, but lost their predictive value in long-term course. HS types had no influence on seizure outcome. There was a significant decline in nonverbal and verbal memory functions postoperatively with no difference between seizure-free and not seizure-free patients.



A: Hippocampus of a healthy control subdividing into dentate gyrus (DG) and subfields of cornu ammonis (CA1-CA4). B: Illustration of HS ILAE type 1 with immunohistochemistry for neural nuclear antigen (NEUN) and glial fibrillary acidic protein (GFAP).

Conclusion: SAHE for patients with MTLE is an effective treatment method with long-term seizure freedom in up to 70%, but there are no reliable predictors for seizure-freedom.

Disclosure: The authors report no conflict of interest.

EPR-091

Evaluation of Pain Sensitivity in Epileptic Patients

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Background and aims: Epilepsy often co-exists with migraine, fibromyalgia, and similar syndromes manifested as chronic pain. There are many similar points between these disorders, such as predisposing factors and therapeutic agents used. This situation suggests common mechanisms that affect neuronal excitability, particularly. We analyzed the pain sensitivity between epileptic patients and healty persons

Methods: This study evaluated the pressure pain threshold, temporal summation, and conditioned pain modulation with a computerized algometer. We made all measurements using the right abductor pollicis brevis muscle in right-hand dominant patients. 20 epileptic patients (according to ILAE criteria and not use antiepileptic drugs in the last three months) were compared with 20 healthy control groups.

Results: Although there was no significant difference between the pressure pain threshold (p=0,2) between epilepsy and control groups, we observed a significant difference in temporal summation (p=0,025) and conditioned pain modulation (p=0.00).

Conclusion: Eloquent differences in temporal summation and conditioned pain modulation show increased central sensitization in epilepsy patients. The underlying mechanism is not clearly known, and this result deserves further research.

Disclosure: Nothing to disclose.

EPR-092

Can We Predict Drug-Resistance in Post-Stroke Epilepsy?

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Italy

Background and aims: Post-stroke epilepsy (PSE) is one of the most common causes of acquired epilepsy. Many investigations have shed light on the risk of epilepsy after stroke, whereas there is little evidence about the factors predicting the response to treatment. The aim of this study was to explore the clinical predictors of pharmaco-resistance in patients with PSE.

Methods: We retrospectively identified adult patients with diagnosis of PSE and no history of seizures before stroke. Data on demographics, clinical history, medications, and seizure occurrence were collected from medical records. Study endpoint was pharmaco-resistance defined as failure of adequate trials of two tolerated and appropriately chosen and used antiseizure medication schedules, whether as monotherapies or in combination, to achieve seizure freedom.

Results: 159 patients with PSE were included. The mean age of the patients at stroke onset was 56.7 (14.9) years, and 104 (65.4%) were males. Overall, 29 (18.2%) participants were pharmaco-resistant. Patients with younger age at stroke onset [odds ratio (OR) 0.97, 95% confidence interval (CI) 0.43–0.99; p=0.049], history of intracerebral hemorrhage (OR 2.60, 95% CI 1.02–6.66; p=0.046), severe stroke (OR 3.69, 95% CI 1.38–9.88; p=0.009) and status epilepticus as initial presentation of PSE (OR 8.87, 2.06–38.12; p=0.003) had a higher likelihood of being refractory to treatment.

Conclusion: Around 20% of patients with PSE were pharmaco-resistant. Age at stroke onset, stroke type and severity, and status epilepticus occurrence as the first late-onset epileptic were independent predictors of drug refractoriness.

Disclosure: Nothing to disclose.

EPR-093

Inflammation- associated microRNAs as biomarkers in adult refractory epilepsy patients under ketogenic diet

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Background and aims: Ketogenic diet (KD) has been increasingly used as treatment of refractory epilepsy in adult patients, with high efficacy and tolerability. Although KD mechanisms-of-action remain poorly understood, it has been suggested that epigenetics, as microRNAs (miRs), may play an important role. This study aimed to analyse the importance of miR-146a and miR-155, previously associated with epilepsy, in the treatment of adult refractory epileptic patients under KD.

Methods: Circulating miR-146a and miR-155 were quantified in 29 adult refractory epileptic patients (16 Females 37.2±15 years-old, disease onset=7.2 ± 8.4 years-old) on KD regimen. Patients were clinical and laboratorial evaluated every three months. Control group comprised 78 healthy individuals (48F; 42.4±10.1 years).

Results: 11 out of 29 patients (38%) responded positively to the treatment, presenting seizure reduction or cognitive improvement. Before diet initiation (T0) miR-146a serum levels were similar in patients and controls. KD induced a serum miR-146a upregulation when compared to controls (M3: p=0.0026, M6: p=0.0051). Circulating miR-155 levels were upregulated, in all considered timepoints, in epileptic patients when compared to controls (T0: p=0.0013; M3: p=0.004, M6: p=0.0009). At M6 miR-155 levels were also increased when compared to M3 (p=0.031).

Conclusion: This preliminary study reinforces the KD potential as a treatment option in adult refractory epilepsy. Our results demonstrate that KD anti-seizure affects can be related to epigenetic reprogramming, namely, microRNAs and it should be investigated whether they can be used as biomarkers of KD efficacy

Disclosure: Funding: LPCE (Liga Portuguesa Contra a Epilepsia) 2020

EPR-094

Acute symptomatic seizures in patients with recurrent ischemic stroke: a retrospective cohort study

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Background and aims: Acute symptomatic seizures are frequent in the setting of acute ischemic stroke (AIS). Recurrent ischemic stroke occurs in more than 10% of cases over one year, despite evidence-based secondary prevention. The risk of seizures during hospital stay in patients with recurrent AIS is unknown.

Methods: Retrospective cohort study including consecutive admissions to a Stroke Unit due to AIS, during a five-year period. Our main objective was comparison of seizure incidence during hospital stay in AIS patients with and without previous stroke. Patients with history of epilepsy were excluded. Logistic regression modelling was performed to identify predictors in middle cerebral artery (MCA) stroke.

Results: We included 1473 patients (1040 with MCA stroke), of which 117 had a recurrent ischemic stroke (43 with MCA stroke). Patients with a first-ever AIS had a risk of seizures similar to patients with recurrent stroke (46 vs. two patients, 4.61% vs. 4.65%, OR 1.08, 95% CI 0.25-4.65). Risk of acute symptomatic seizures was also similar (4.11% vs 4.65%, OR 1.22, 95% CI 0.29–5.27). Older age, female sex, and hemorrhagic transformation were predictors of seizures in patients with a first MCA ischemic stroke, but not in patients with recurrent stroke. Electrographic characteristics were similar between the two groups in patients who had an electroencephalogram (46 with first stroke, four with recurrent stroke).

Conclusion: History of previous stroke was not associated with an increased risk of seizures during hospital stay. Larger, prospective studies, with extensive electro-physiological evaluation, are needed to explore the impact of stroke recurrence on seizure risk.

Disclosure: The authors have no conflicts of interest to declare.

Headache and Pain 2

EPR-095

Autonomic Function Testing in Migraine – A Systematic Review and Meta-analysis

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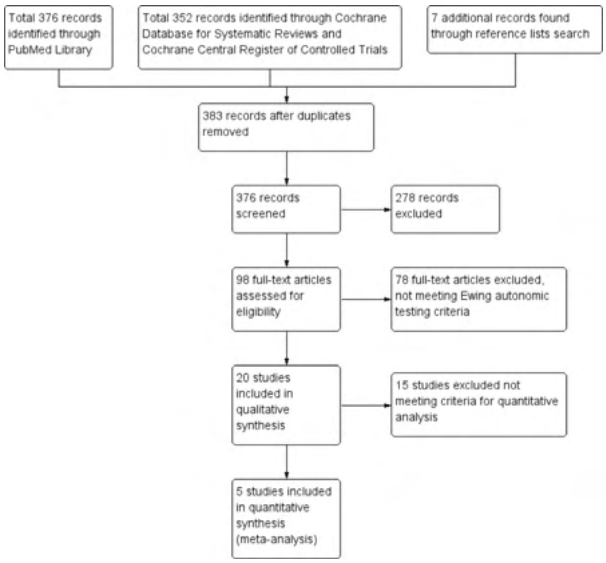
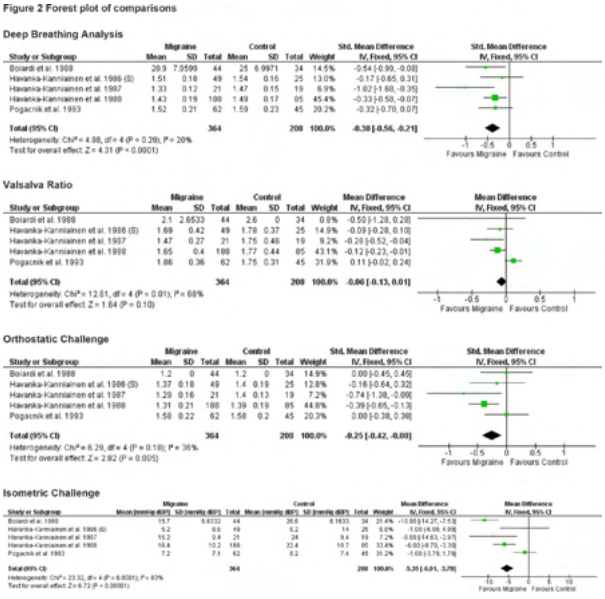
Background and aims: Research, using autonomic tests, has aided in our ability to evaluate autonomic dysfunction in patients with migraine. Our objective was to perform a systematic review and meta-analysis of studies comparing autonomic function in migraineurs and healthy subjects.
Methods: We searched PubMed library, Cochrane Database for Systematic Reviews and Cochrane Central Register of Controlled Trials for results up to January 2021 and evaluated full text articles for 98 of 376 search results. Five articles met all selection criteria. The respective deep breathing, Valsalva maneuver, orthostatic and isometric challenge results of these five articles were pooled together. All analyses were carried out using Review Manager 5.4.



Flow chart of search methodology and results. Autonomic Function Testing in Migraine

Results: Migraine patients, collectively, had lower autonomic test results compared with healthy controls. The standardized mean difference (SMD) was -0.38 (95% confidence interval (CI) -0.56 to -0.21) for deep breathing, and -0.25 (CI -0.42 to -0.08) for orthostatic testing. In the isometric hand grip challenge, diastolic blood pressure showed a mean difference (MD) of -5.35mmHg (CI -6.91 to -3.79). The Valsalva ratio did not differ in patients and controls. The heterogeneity was low for deep breathing and orthostatic testing (I^2 =20% and I^= 6%, respectively) and relatively high for isometric testing and Valsalva maneuver (I^2 = 83% and I^2=68%, respectively).



Forest plot of comparisons: Migraineurs VS Controls, Deep Breathing, Valsalva Maneuver, Orthostatic Challenge and Isometric Challenge

Conclusion: Autonomic dysfunction can be identified in migraineurs when compared to healthy controls. These findings indicate the importance to evaluate autonomic function in migraineurs - especially, as new prophylactic migraine therapies (such as anti-CGRP-mAbs) may affect function of the autonomic nervous system.
Disclosure: Nothing to disclose

EPR-096

Secondary Cluster Headache: description of five cases

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Background and aims: Cluster headaches (CH) are clinically defined by the presence of severe strictly unilateral headache, lasting between 15–180 minutes and accompanied by ipsilateral autonomic symptoms. CH belong to the group of trigeminal autonomic cephlalgias (TACs), covered in the section of primary headaches of the 3rd edition of the International Classification of. Headache Disorders (ICHD-3). However, a number of cases of symptomatic cluster headaches have been described in the last decades.

Methods: We describe a case series of five patients with CH according to ICHD-3 diagnostic criteria secondary to diverse causes.

Results: Five patients were diagnosed with symptomatic CH secondary to different etiologies: arteriovenous malformation, multiple sclerosis, dural arteriovenous fistula, traumatic brain injury and macroprolactinoma. All of them showed atypical characteristics at the time of diagnosis or during the disease course.

Conclusion: Neuroimaging is still necessary in the diagnostic study of TAC to exclude secondary causes and should be a priority in the cases with atypical features. Changes in symptomatology or in its temporal pattern, alterations in clinical examination or lack of response to specific therapy are considered red flags and MRI including magnetic resonance angiography should be performed.

Disclosure: I have nothing to disclose.

EPR-097

Safety Findings from CENTURION, a Phase 3 Consistency Study of Lasmiditan for the Acute Treatment of Migraine

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Background and aims: Lasmiditan is a selective 5-HT_{1F} receptor agonist for the acute treatment of migraine in adults. We present safety findings from the placebo-controlled, double-blind Phase 3 study, of lasmiditan treatment across 4 attacks (CENTURION).

Methods: Patients were randomised 1:1:1 to lasmiditan 200mg (LTN200), LTN100, or a control group that received placebo for 3 attacks and LTN50 for either the third or fourth attack (1:1). Safety analyses were conducted for patients who took ≥1 dose of study drug.

Results: In CENTURION, 1,471 patients treated 4,494 attacks. The incidences of treatment-emergent serious adverse events (SAEs) were placebo, n=2 (0.4%); LTN100, n=1 (0.2%); LTN200, n=2 (0.4%); no specific SAE was reported in more than one patient. There were no deaths or major cardiovascular events. The most common treatment emergent adverse events (TEAEs) with lasmiditan were dizziness, paresthesia, fatigue, nausea, vertigo, and somnolence; the vast majority were mild or moderate in severity. The incidences of these TEAEs were highest during the first attack and decreased during subsequent attacks. Median durations of common TEAEs with lasmiditan ranged from 1.1 to 5.5 hours and was higher in the first compared to the fourth attack, except for fatigue and somnolence. Findings are tabulated for dizziness, the most common TEAE.

Incidence , onset and duration of dizziness by attack (safety population)

	n (%)		Onset (hours), median (IQR)		Duration (hours), median (IQR)	
	Placebo	Lasmiditan pooled	Placebo	Lasmiditan pooled	Placebo	Lasmiditan pooled
Attack 1	23 (4.6)	212 (21.8)	1.7 (0.5-3.8)	0.7 (0.4-1.2)	4.3 (1.0-9.5)	2.5 (1.0-5.8)
Attack 2	8 (1.8)	124 (15.3)	1.0 (0.1.-1.8)	0.7 (0.4-1.0)	3.0 (0.8-4.6)	3.0 (1.2-6.0)
Attack 3	12 (3.2)	87 (13.6)	1.1 (0.4-1.9)	0.5 (0.4-1.0)	2.5 (0.3-3.8)	2.0 (1.0-4.7)
Attack 4	12 (4.5)	62 (12.6)	0.6 (0.4-1.0)	0.7 (0.5-1.0)	0.9 (0.5-1.4)	1.8 (1.0-3.2)

IQR, interquartile range; n, number of patients with dizziness
Lasmiditan pooled = findings from lasmiditan 100 and 200 mg doses combined
Dizziness considered those events occurring up to 48 hours after study drug administration
Time to onset is calculated as the difference between TEAE start time and the indicated dosing time. Events missing start times/dates or dosing times/dates are not included for analysis. Only time to onset of first occurrence during the selected attack of the same patient for the same event was used.

Conclusion: In this blinded, controlled, multiple-attack study, lasmiditan was associated with generally mild or moderate CNS-related TEAEs of short duration. TEAEs tended to decrease in frequency across the four attacks. There were no new safety findings compared with previous single attack studies.

Disclosure: The CENTURION study was sponsored by Eli Lilly and Company.

EPR-098

Symptomatic migraine: A systematic review of clinical features and etiology

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Background and aims: It is currently not clear whether migraine truly can be caused by an underlying condition or pathology. Characterization of the etiology and clinical features of possible symptomatic migraine is of significant clinical importance and further may help elucidate the pathophysiology of migraine. In this review, we systematically assessed reports of putative "symptomatic migraine" in the literature with emphasis on clinical features and etiology.
Methods: We devised operational diagnostic criteria for "symptomatic migraine" and "possible symptomatic migraine". PubMed was searched for reports of symptomatic migraine from inception to March 2020. Relevant references in the articles were also included. Papers were systematically reviewed by two independent reviewers for detailed clinical features of migraine as well as the proposed underlying conditions and the effects of treatment of these conditions.
Results: Our search retrieved 1,726 items. After screening, 90 case papers (comprising 120 individual cases) and 19 group papers were reviewed in detail. Eleven patients with migraine with aura fulfilled our working criteria for symptomatic migraine and 39 patients fulfilled our criteria for possible symptomatic migraine. Most common etiologies were arteriovenous malformations, carotid stenosis, dissection or aneurysm, brain infarctions, meningioma, and various intra-axial tumors.
Conclusion: Symptomatic migraine with aura, indistinguishable from idiopathic migraine with aura, may occur due to cortical lesions or microembolization. We found no clear evidence supporting the existence of symptomatic migraine without aura
Disclosure: AVT and MTS report no disclosures. AH Received honoraria for lecturing and/or writing from Allergan, Novartis, Teva, (no space for remaining) MA has received personal fees from Allergan...

EPR-099

Idiopathic intracranial hypertension without papilledema: a single-center study

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Background and aims: Idiopathic intracranial hypertension without papilledema (IIHWP) is a rare form of chronic headache, usually misdiagnosed in the absence of the specific radiological signs of idiopathic intracranial hypertension (IIH). In this study, we aimed to assess the clinical features and neuroradiological signs in patients with IIHWP.
Methods: A retrospective study is conducted between January 2015 and December 2020, including patients, diagnosed IIH, who didn't have papilledema in their optic fundus in order to describe the clinical and radiological features as well as the prognosis of patients with IIHWP and determine whether they fulfill the Friedman diagnostic criteria of IIHWP. All patients underwent a lumbar puncture with opening pressure (OP) measurement and an MRI.
Results: Among 67 diagnosed IIH, nine female patients (13%) had IIHWP with a mean age at onset of 37,7±9 years. Neurological examination was unremarkable in seven patients and showed a bilateral abducens palsy in two patients. Brain MRI didn't show any abnormalities in most of the cases (66%), while two patients had an empty sella and one patient had three radiological criteria of IIH. Cerebrospinal fluid (CSF) OP was over 25cmH_2O in all patients (mean CSF OP: 41±15 cmH2O). According to Friedman's diagnostic criteria, only three patients are diagnosed with IIHWP. At six months follow-up, only six patients experienced an improvement of their symptoms.
Conclusion: IIHWP is a challenging clinical entity and diagnosis is difficult due to the absence of papilledema. Although it is rare, it should be considered whenever an atypical chronic headache is encountered.
Disclosure: No disclosure

EPR-100

Atogepant Improved Measures of Functioning Using AIM-D and HIT-6 in a 12-Week Phase 3 Trial for Migraine Prevention

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Background and aims: Atogepant is an oral calcitonin gene–related peptide receptor antagonist under development for the preventive treatment of migraine.
Methods: The phase 3, multicenter, randomized, double-blind, parallel-group, placebo-controlled ADVANCE (NCT03777059) trial evaluated the efficacy and safety of atogepant for preventive migraine treatment in participants with 414 migraine days/month. Participants received atogepant 10mg, 30mg, 60mg, or placebo once daily for 12 weeks. Patient-reported outcomes included: Activity Impairment in Migraine-Diary (AIM-D), consisting of two domains (0–100; lowest-greatest impact): Performance of Daily Activities (PDA) and Physical Impairment (PI); and Headache Impact Test (HIT-6).
Results: Of 910 participants randomized, 902 received treatment (mean age: 41.6 years; 89% female); 873 were in the modified intent-to-treat population (atogepant 10mg, n=214; 30mg, n=223; 60mg, n=222; placebo, n=214). Compared with placebo, all atogepant groups demonstrated improvements in PDA and PI scores across the 12-week treatment period. For both AIM-D domains, differences were significant for atogepant 60mg and 30mg (least squares mean difference [LSMD] vs placebo: PDA, 60mg: 3.32, 30mg: –2.54; PI, 60mg: 2.46, 30mg: 1.99). Improvements in PDA and PI domains for atogepant 10mg did not reach significance vs placebo (LSMD: 1.19 and 1.08, respectively). All atogepant groups demonstrated significant improvement in HIT-6 scores vs placebo at weeks 4, 8, and 12. Significantly greater proportions of atogepant- vs placebo-treated participants were HIT-6 responders (≥5 point decrease) with all atogepant doses, except 30mg at week 4.
Conclusion: Atogepant significantly improved performance in daily activities and reduced physical impairment and impact of headaches, confirming its role as a promising migraine treatment.
Disclosure: This study was supported by Allergan (prior to its acquisition by AbbVie).

EPR-101

Efficacy and Safety of Eptinezumab Initiated During a Migraine Attack: Results from the RELIEF Study

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Background and aims: Eptinezumab is an approved migraine preventive treatment, with demonstrated rapid onset of preventive benefit. RELIEF evaluated the efficacy and safety of eptinezumab when initiated during a migraine attack.
Methods: RELIEF (NCT04152083; parallel-group, double-blind, placebo-controlled) randomized adults (18–75y) with migraine, on 4–15d/mo in 3mo prior to screening, to eptinezumab 100mg or placebo, administered IV within 1–6h of moderate to severe migraine attack onset. Co-primary efficacy endpoints were time to headache pain freedom and time to absence of most bothersome symptom (MBS; nausea, photophobia, or phonophobia). Secondary endpoints included headache pain freedom and absence of MBS at 2h and 4h, and use of rescue medication within 24h. Safety was also assessed.
Results: Eptinezumab-treated (n=238) compared with placebo patients (n=242) achieved significantly faster headache pain freedom (median 4h vs 9h, respectively; hazard ratio=1.54, p=0.0006) and absence of MBS (median 2h vs 3h; hazard ratio=1.75, p<0.0001). At 2h, 23.5% and 12.0% (p=0.0009) of patients receiving eptinezumab and placebo, respectively, reported headache pain freedom, and 55.5% and 35.8% (p<0.0001) reported absence of MBS. Results remained significant at 4h. Significantly fewer eptinezumab-treated patients used rescue medication within 24h vs placebo patients (31.5% vs 59.9%; p<0.0001). Treatment-emergent adverse events occurred in 10.9% eptinezumab-treated and 10.3% placebo patients; no serious adverse events occurred.
Conclusion: Infusion of the preventive migraine treatment, eptinezumab, during a migraine attack resulted in rapid and sustained freedom from headache pain and MBS compared with placebo, starting 2h post-infusion, and decreased need for acute medication within 24h post-infusion. No notable safety findings were identified.
Disclosure: H. Lundbeck A/S, Copenhagen, Denmark

EPR-102

Total pain burden in patients with treatment-resistant migraine: effects of galcanezumab in the CONQUER Phase 3b trial

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Background and aims: Total pain burden, a composite measure encompassing frequency of migraine headache days, duration, and severity, was previously used to characterize response to galcanezumab in patients with migraine. Here it is used to measure response in patients with treatment-resistant migraine.

Methods: CONQUER trial patients (n=458), 18–75 years old with 2–4 prior migraine preventive treatment category failures, were randomised (1:1) to monthly placebo or galcanezumab 120mg with 240mg loading dose. For each patient, monthly total pain burden in severity-weighted hours was calculated by multiplying daily migraine headache duration (hours) by maximum severity (0=none, 1=mild, 2=moderate, 3=severe) for each migraine day, then summing daily scores for the monthly score. Changes from baseline in monthly total pain burden across Months 1–3 were analysed post hoc using mixed-model repeated measures. Spearman correlations between total pain burden and Migraine Specific Quality-of-Life Questionnaire (MSQ) and Migraine Disability Assessment Scale (MIDAS) were assessed at baseline.

Results: Mean (SD) baseline monthly total pain burden was 192.1 (158.3) and 188.2 (197.4) severity-weighted hours for galcanezumab-treated and placebo-treated patients, respectively. Across the 3-month double-blind period, galcanezumab-treated patients experienced significantly greater mean reductions from baseline in monthly total pain burden compared with placebo-treated patients, both for mean change (galcanezumab: -82.7, placebo: -15.8, $p<0.001$) and percent change (galcanezumab: -38.6%, placebo: 9.4%, $p<0.001$) (Table 1). Furthermore, baseline total pain burden correlated with MSQ score ($r=-0.39$) and MIDAS score ($r=0.40$), suggesting good association of total pain burden with quality-of-life outcomes.

Total Pain Burden Outcome	Overall LS Mean Change (SE) PBO N=228	GMB N=230	Difference to PBO (95% CI)	p-value vs. PBO
Change from baseline	-15.8 (7.5)	-82.7 (7.5)	-66.8 (-85.5, -48.2)	<0.001
% change from baseline	9.4% (5.7)	-38.6% (5.7)	-48.1% (-62.3, -33.9)	<0.001

Abbreviations: CI, confidence interval; GMB, galcanezumab; LS, least squares; N, number of patients; PBO, placebo; SE, standard error

Table 1. Galcanezumab-treated patients experienced significantly greater mean decreases in monthly total pain burden outcome measures (severity-weighted hours) over three months of double-blind treatment.

Conclusion: Total pain burden may be an additional meaningful measure for clinicians when discussing migraine preventive therapy.

Disclosure: This study was sponsored by Eli Lilly and Company.

Movement disorders 2

EPR-103

Part of personality is predictive of quality-of-life outcome after deep brain stimulation in Parkinson's disease

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Background and aims: At the stage of motor fluctuations, Parkinson's disease (PD) strongly impacts Quality of Life (QoL) of patients. Therefore, patients can be treated by Deep Brain Stimulation of the Sub-Thalamic Nucleus (DBS-STN) which highly improves their motor state. Nonetheless, some patients are still unsatisfied after this invasive treatment and do not enjoy the objective benefits of it. Therefore, our objective was to evaluate personality dimensions as a potential predictor of QoL evolution after one year of DBS-STN, as a marker of patients' satisfaction.
Methods: Data of 303 PD patients were used from the PREDI-STIM cohort, with QoL assessed by the PDQ-39 (Parkinson's disease Questionnaire-39) before and after one year of DBS-STN, and personality evaluated by the TCI (Temperament and Character Inventory) only before stimulation. Linear regression models were done between these two variables.
Results: Three personality dimensions from the TCI were found significantly and positively associated with better PDQ-39 scores after DBS-STN: namely the Novelty Seeking, one subdimension of Harm Avoidance (the Fatigability) and the Cooperativeness.
Conclusion: PD patients with higher Novelty Seeking, Fatigability and Cooperativeness scores had a better improvement of their QoL after one year of DBS-STN. Being motivated by novelty and having a good social maturity (listening to others, etc.) are important factors to respond positively to DBS. Moreover, we hypothesize that the decrease of Fatigability after stimulation is beneficial to the patients. Therefore, PD educational program could be proposed to patients undergoing DBS to prepare them to the abrupt changes induced by it.
Disclosure: The study was funded by the France Parkinson charity and French Ministry of Health (PHRC national 2012). This is an ancillary study to Protocol ID: 2013-A00193-42; ClinicalTrials.gov: NCT02360683.

EPR-104

Long-term effects of transcranial magnetic stimulation on speech of patients with Parkinson's disease

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Background and aims: Hypokinetic dysarthria is a common symptom of Parkinson's disease (PD) that does not respond well to PD treatments. We examined the long-term effects of multiple-session repetitive transcranial magnetic stimulation on hypokinetic dysarthria in PD.

Methods: A randomized parallel-group sham stimulation-controlled design was used. Patients were assigned to ten sessions of real (1 Hz) or sham stimulation over the right superior temporal gyrus (STG). Stimulation effects were evaluated at weeks 2, 6, and 10 after the baseline assessment. Prosody, articulation and speech intelligibility were quantified by speech therapist using a validated tool (Phonetics score). Activations of the speech network regions, structural and functional connectivity were analyzed.

Results: Altogether 33 PD patients completed the study. Linear mixed model showed significant time-by-group interactions for the Phonetics score (p=0.040). Real as compared to sham stimulation led to increased activations of the left orofacial sensorimotor cortex (OFSM1) (p=0.032) and left caudate nucleus (p=0.029) and to increased intrinsic connectivity of the OFSM1 with the stimulated area (p=0.045). A significant positive correlation was found between the temporal evolution of the Phonetics score and the STG-OFSM1 functional connectivity changes in the real stimulation group (r=0.449, p=0.013). DTI analysis revealed that real as compared to sham stimulation significantly increased fractional anisotropy and decreased mean diffusivity in the left anterior arcuate fasciculus (p=0.002; p=0.036).

Conclusion: This is the first study to show the long-lasting effects of low-frequency rTMS on hypokinetic dysarthria in PD.

Disclosure: Nothing to disclose.

EPR-105

How to assess the impact of DBS on voluntary postural control in PD patients

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Background and aims: The disturbance of voluntary postural control (VPC) develop and progress in PD patients. It is known that DBS has different effects on VPC in PD patients. Stabilometry with biological feedback is used to objectify violations of VPC in PD.

Methods: We examined 59 (40 with tremor, 19 with hypokinesia and rigidity) PD patients during DBS. 31 male and 28 female, median age 58[54;62] years, 46 patients–II stage of H&Y, 13–III. 46 patients with DBS STN, 10 – DBS GPi, 3 – DBS Vim. A comprehensive indicator was used to assess the VPC. It consists of score number 13, 14, 15, 29, 30 items of UPDRS. We used computer stabiloanalizator with biofeedback. Test was carried out with a stepped exposure, which assessed the displacement of the patient's pressure center as a response to an voluntary change of target position on the screen. Patients moved the PC forward (compensation stage), then returned to the initial position. The speed of throw (ST), mm/sec and reaction time (RT), sec was evaluated at the compensation stage.

Results: Statistically significant difference by Friedman ANOVA of PIGD in off-med during two years of DBS ANOVA X^2=10,05, p<0,00004 (figure 1). Increase of ST indicator revealed after one month (W-test, p=0,0004), one year (W, p=0,018), two year of DBS (W, p=0,028). Decrease of RT indicator revealed after one month (W-test, p=0,0007), one year (W, p=0,043), two year of DBS (W, p=0,028).

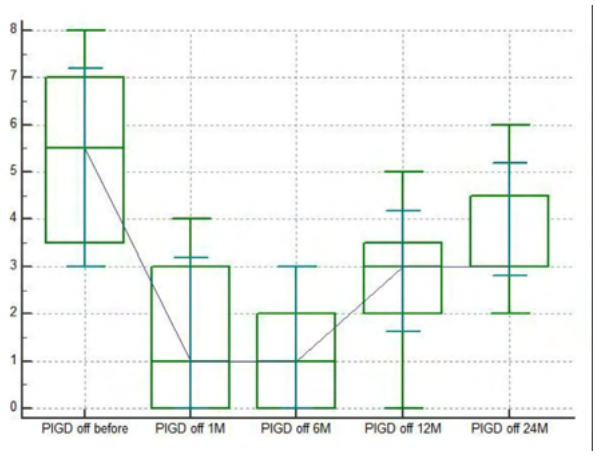

Figure 1. Friedman ANOVA of PIGD in off-med during two years of DBS

Conclusion: The results indicate an improvement in speed and time parameters of VPC over two years DBS in the study group.

Disclosure: No disclosure

EPR-106

Influence of levodopa daily dose in Opicapone effectiveness in Parkinson's: the real-world OPTIPARK study

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Background and aims: Opicapone (OPC) proved to be effective in treating end-of-dose motor fluctuations (MF) in Parkinson's disease (PD) patients [1,2]. The OPTIPARK study evaluated OPC 50mg in a heterogeneous population of patients treated in real-world conditions [3].

Methods: OPTIPARK was a prospective, open-label, single-arm trial conducted in Germany and the UK. Patients with MF received OPC 50mg in addition to current antiparkinsonian treatment. Primary efficacy 3-month endpoint was Clinician's-Global-Impression-of-Change (CGI-C). Secondary efficacy endpoints included Patient's-CGI-C (PGI-C), 8-item PD Questionnaire (PDQ-8), Unified PD Rating Scale (UPDRS) and Non-Motor Symptoms Scale (NMSS). Safety assessments included evaluation of treatment-emergent adverse events (TEAEs). This post-hoc analysis evaluated the influence of levodopa daily dose at baseline in patients who completed the study for each outcome.

Results: 393 (82.4%) patients completed the 3-month endpoint (completers-set, Table 1). Of these, patients taking 'low-levodopa' daily dose experienced greater very-much/much improvement on CGI-C and PGI-C, when compared to patients taking 'high-levodopa' daily dose (Table 2). Similarly, patients taking 'low-levodopa' daily dose reported greater improvements on both UPDRS-II and III, quality-of-life (PDQ-8) and non-motor-symptoms (NMSS) (Table 3). Lower incidence of TEAEs considered at least possibly related to OPC were also reported for patients taking 'low-levodopa' daily dose (Table 3).

Table 1. Baseline characteristics (Completer-Set)

Category	Levodopa amount at baseline			
	< 500 mg	≥ 500 mg	< 750 mg	≥ 750 mg
	N=157	N=236	N=311	N=82
Age, mean (SD)	66.9 (9.4)	67.4 (8.8)	67.1 (9.2)	67.5 (8.4)
Male, n (%)	88 (56.1)	169 (71.6)	194 (62.4)	63 (76.8)
PD duration, mean (SD) years	7.5 (4.5)	9.0 (4.6)	8.1 (4.6)	9.5 (4.5)
Onset of MF, mean (SD) years	2.1 (3.3)	2.6 (2.8)	2.1 (2.9)	3.3 (3.1)
Ldopa amount, mean (SD) mg	330 (90)	710 (196)	461 (156)	927 (164)

SD, standard deviation; PD, Parkinson's Disease; MF, motor fluctuations

Table 2. CGI-C and PGI-C results after 3 months (Completer-Set)

Category	Levodopa amount at baseline			
	< 500 mg	≥ 500 mg	< 750 mg	≥ 750 mg
	N=157	N=236	N=311	N=82
	n (%)	n (%)	n (%)	n (%)
CGI-C				
Not assessed	-	-	-	-
Very much improved	12 (7.6)	18 (7.6)	25 (8.0)	5 (6.1)
Much improved	71 (45.2)	96 (40.7)	139 (44.7)	28 (34.1)
Minimally improved	49 (31.2)	74 (31.4)	90 (28.9)	33 (40.2)
No change	21 (13.4)	35 (14.8)	41 (13.2)	15 (18.3)
Minimally worse	3 (1.9)	10 (4.2)	12 (3.9)	1 (1.2)
Much worse	1 (0.6)	2 (0.8)	3 (1.0)	-
Very much worse	-	1 (0.4)	1 (0.3)	-
PGI-C				
Not assessed	-	-	-	-
Very much improved	12 (7.6)	18 (7.6)	26 (8.4)	4 (4.9)
Much improved	73 (46.5)	86 (36.4)	131 (42.1)	28 (34.1)
Minimally improved	41 (26.1)	72 (30.5)	84 (27.0)	29 (35.4)
No change	23 (14.6)	35 (14.8)	46 (14.8)	12 (14.6)
Minimally worse	6 (3.8)	19 (8.1)	19 (6.1)	6 (7.3)
Much worse	2 (1.3)	4 (1.7)	4 (1.3)	2 (2.4)
Very much worse	-	2 (0.8)	1 (0.3)	1 (1.2)

CGI-C, Clinician's Global Impression of Change; PGI-C, Patient's Global Impression of Change

Table 3. Secondary, after 3 months, and safety outcomes (Completer-Set)

Category	Levodopa amount at baseline			
	< 500 mg	≥ 500 mg	< 750 mg	≥ 750 mg
	N=157	N=236	N=311	N=82
	mean (SD)	mean (SD)	mean (SD)	mean (SD)
UPDRS II (at ON stage)	-1.9 (3.0)	-1.4 (4.1)	-2.0 (3.7)	-0.4 (3.5)
p-value	*<.0001*	*<.0001*	*<.0001*	*0.2983*
UPDRS III	-4.9 (7.5)	-4.4 (8.5)	-4.9 (8.3)	-3.5 (7.0)
p-value	*<.0001*	*<.0001*	*<.0001*	*<.0001*
PDQ-8	-4.1 (11.4)	-3.0 (13.7)	-3.7 (12.6)	-2.6 (13.8)
p-value	*<.0001*	*0.0008*	*<.0001*	*0.0919*
NMSS	-7.4 (18.4)	-6.4 (20.6)	-7.3 (19.0)	-4.8 (22.3)
p-value	*<.0001*	*<.0001*	*<.0001*	*0.0561*
Any TEAE, n (%)	97 (61.8)	184 (78.0)	210 (67.5)	71 (86.6)
At least possibly related[a] TEAEs, n (%)	54 (34.4)	100 (42.4)	112 (36.0)	42 (51.2)

SD, standard deviation; UPDRS, Unified Parkinson's Disease Rating Scale; PDQ-8, 8-item Parkinson's Disease Questionnaire; NMSS, Non-Motor Symptoms Scale; p-values obtained through Student's t-test for the change from baseline; [a]relationship to study medication reported as 'possible', 'probable', 'definite' or missing; TEAE, treatment-emergent adverse event (with onset or worsening after first opicapone intake until study termination, either regularly or prematurely)

Conclusion: These findings indicate that PD patients with MF and taking 'low-levodopa' daily dose (representative of recent fluctuators) may have an added benefit from using OPC 50 mg as adjunctive therapy to levodopa.

Disclosure: 1.Ferreira et al., Lancet Neurology 2016;15(2):154-165; 2.Lees et al., JAMA Neurol. 2017;74(2):197-206; 3.Reichmann et al., Transl Neurodegener. 2020;9(1):9

EPR-107

INSIGHTS: Levodopa-Carbidopa Intestinal Gel Therapy Vs Optimised Medical Treatment on Non-Motor Symptoms in Advanced PD

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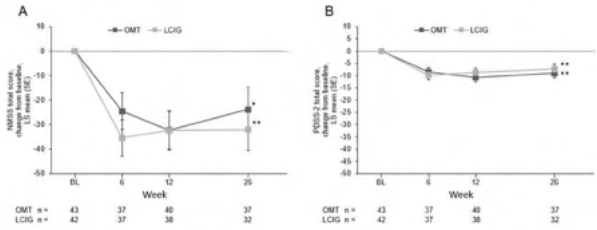
Background and aims: Non-motor symptoms (NMS) are common and reduce quality of life in Parkinson's disease (PD). We evaluated effects of levodopa-carbidopa intestinal gel (LCIG) versus optimised medical treatment (OMT) on NMS in patients with advanced PD (APD).

Methods: INSIGHTS was a Phase 3b, open-label, randomised, multicentre study (NCT02549092). Patients with APD received LCIG or OMT (26 weeks). Primary NMS measures (NMS Scale [NMSS], PD Sleep Scale [PDSS-2]), secondary measures (Unified PD Rating Scale [UPDRS], Clinical Global Impression of Change [CGI-C], PD Questionnaire-8 [PDQ-8]), and safety were assessed.

Results: Of the 89 randomised patients, 87 were included in analysis (LCIG, n=43; OMT, n=44). There were no statistically significant differences in NMSS or PDSS-2 total score changes (baseline to Week 26) between LCIG and OMT (least squares mean of difference [standard error]=–8.2 [9.9], p=0.410 [Figure 1A] and 1.6 [2.4], p=0.509 [Figure 1B]). Results from additional and sensitivity analyses were consistent. Within-group changes from baseline at Week 26 were significant for NMSS (LCIG, p<0.001; OMT, p=0.005) and PDSS-2 (LCIG, p<0.001; OMT, p<0.001). Nominal significance was demonstrated for between-group treatment differences for UPDRS Part II (p=0.006) and CGI-C (p<0.001, Week 26) in favor of LCIG (Table 1). There was no significant difference in PDQ-8 (p=0.291) (Table 1). Adverse events (AEs) were mostly mild to moderate; most frequent serious AEs with LCIG were pneumoperitoneum (n=2) and stoma site infection (n=2).



LCIG, levodopa-carbidopa intestinal gel; LS, least squares; NMSS, Non-Motor Symptom Scale; OMT, optimised medical treatment; PDSS-2, Parkinson's Disease Sleep Scale; SE, standard error.

*Significance of within-group change from baseline at Week 26, p<0.01; **Significance of within-group change from baseline at Week 26, p<0.001.

LCIG versus OMT changes from baseline in total scores were analysed by mixed-effects model for repeated-measures.

Figure 1. Least Squares Mean Change from Baseline for NMSS (A) and PDSS-2 (B) Total Scores Over the 26-Week Treatment Period (Intent-to-Treat Dataset)

			Observed Mean (SD)				LS Difference from OMT		
Endpoints[a]	Group	n[b]	Baseline	Change to Week 26	LS mean (SE)	Within group P-value	LS mean (SE) of difference	95% CI	P-value
UPDRS Part II (ADL) score	OMT	44	17.5 (7.0)	−0.1 (4.7)	0.5 (0.9)	0.549	−2.8 (1.0)	(−4.8, −0.8)	0.006[d]
	LCIG	43	16.7 (7.1)	−2.6 (5.7)	−2.3 (0.9)	0.012			
PDQ-8 summary index	OMT	44	44.5 (17.3)	−6.3 (19.6)	−1.8 (3.0)	0.556	−3.8 (3.6)	(−11.0, 3.3)	0.291
	LCIG	43	39.7 (17.3)	−7.2 (18.3)	−5.6 (3.0)	0.064			
CGI-C score	OMT	43		4.7 (1.2)[c]	4.9 (0.3)	<0.001	−2.3 (0.3)	(−2.8, −1.8)	<0.001[d]
	LCIG	40		2.4 (1.2)[c]	2.5 (0.2)	<0.001			

[a]Analyses for all continuous efficacy endpoints are for the change from baseline value (with the exception of CGI-C, which is the score at Week 26). Results for all efficacy variables are based on MMRM analysis with the exception of CGI-C which is based on the ANOVA model; [b]Number of subjects in the intent-to-treat dataset with baseline value; [c]Week 26 CGI-C score; [d]Statistical significance was not achieved after multiplicity adjustment.

ADL, activities of daily living; ANOVA, analysis of variance; CGI-C, Clinical Global Impression of Change; CI, confidence interval; LCIG, levodopa-carbidopa intestinal gel; LS, least squares; MMRM, mixed-effects model repeated-measures; OMT, optimised medical treatment; PDQ-8, Parkinson's Disease Questionnaire-9 item summary index; SD, standard deviation; SE, standard error; UPDRS, Unified Parkinson's Disease Rating Scale.

Table 1. Results of Key Secondary Endpoints

Conclusion: Though both groups significantly improved, no significant differences for LCIG vs OMT were shown in NMSS or PDSS-2. AEs with LCIG were consistent with the known safety profile.

Disclosure: AbbVie funded the research for this study and participated in the study design; study research; collection, analysis, and interpretation of data; and writing, reviewing, and approving this abstract for submission.

EPR-108

Autonomic dysfunction: a non-motor symptom in patients with idiopathic cervical dystonia

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Background and aims: A case-control study to investigate the possible autonomic nervous system involvement in patients with idiopathic cervical dystonia using clinical and neurophysiological evaluation. Second, the study aims to identify the possible relation between autonomic dysfunction and cervical dystonia severity.

Methods: We administered Composite Autonomic System Scale 31 and power spectral analysis applied to Laser Doppler Flowmetry of right and left index to 20 patients with idiopathic cervical dystonia and 20 healthy subjects. Power spectral analysis, high-frequency and low-frequency oscillations, and low frequency/high-frequency ratio of Laser Doppler Flowmetry were measured at rest, after both parasympathetic (6 deep breathing) and sympathetic activation (isometric handgrip and mental arithmetic calculation).

	CASES (N=20)	CONTROLS (N=20)
Sex (F/M)	12/8	12/8
Mean age (years)	56.9 (11.1)	56.9 (11.1)
Mean age at disease onset (years)	41.3 (11.6)	NA
Disease duration (years)	15.7 (6.4)	NA
Duration of Botulinum toxin treatment (years)	12.3 (6.7)	NA
Smokers (number)	3	6
Coffe intake (number of subjects)	13	16
Alcohol use (number of subjects)	13	17
Positive familiar history of dystonia and/or depression and/or dementia (number of subjects)	5	7

Value are expressed as mean ± DS

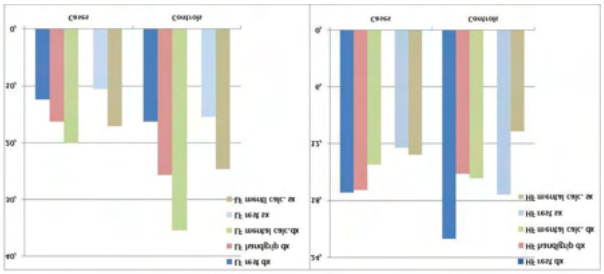
Population characteristics

Results: Patients showed more significant autonomic symptoms on the clinical scale than controls ($p<0.05$), especially on orthostatic hypotension and gastroenteric domains. At rest, patients had lower high-frequency power than healthy subjects, reaching a statistically significant difference among the group with age equal or higher than 60 years old ($p<0.05$). The latter patients' group had a lower low-frequency/high-frequency ratio than controls both at rest and after the mental calculation ($p<0.05$). In contrast, all patients showed a lower ratio during handgrip. These sympathetic conditions induced a similar low-frequency oscillatory component increase in patients and controls. Differently, the high frequency remained unchanged in patients and decreased in controls. No differences were detected during deep-breathing; both groups showed significant high-frequency oscillations increase.

Condition		LF (ds/ss)	HF (ds/ss)	LF/HF ratio (ds/ss)
Rest				
	Cases	12.35 (9.52-33.22)/10.55 (6.82-29.85)	17.20 (10.50-34.62)/12.40 (8.05-25.22)	0.94 (0.32-2.04)/ 0.85 (0.28-3.57)
	Controls	16.35 (10.47-60.52)/15.45 (9.07-21.40)	22.05 (17.62-25.57)/17.40 (7.85-23.75)	1.07 (0.39-3.60)/1.07 (0.39-3.60)
	Cases ≥ 60 yo	12.90 (11.40-28.50)/10.10 (7.40-15.95)	**11.25** (20.90-39.00)/ **10.2** (8.35-30.70)	**0.64** (0.25-1.34)/ **0.29** (0.26-3.00)
	Controls ≥ 60 yo	14.00 (9.85-22.05)/ 18.6 (10.75-19.90)	**21.40**(17.30-23.40)/**19.00**(17.10-22.60)	**1.50** (1.27-2.90)/ **3.10** (1.15-3.98)
Mental calculation				
	Cases	20.05 (9.56-29.3)/ 17.45 (11.33-26.8)	14.2 (8.2-24.8)/ 13.2 (7.07-26.52)	1.10 (0.46-3.67)/ 1.31 (0.45-3.62)
	Controls	35.5 (16.6-44.63)/ 24.7 (13.78-53.23)	15.65 (10.5-28.03)/ 10.7 (7.34-23.76)	1.65 (0.90-3.57)/ 3.84 (0.86-4.81)
	Cases ≥ 60 yo	19.5 (5.1-30.85)/ 18.6 (14.85-32.5)	**18.8** (11.55-29.2)/ 14.1 (7.35-22.65)	**1.04** (0.23-1.36)/ **1.24** (0.27-1.51)
	Controls ≥ 60 yo	20.9 (17.65-36.6)/25.4 (19.3-47.35)	14.9 (11.85-15.65)/ 11 (9.1-14.8)	**3.52** (1.83-4.59)/ **4.45** (3.06-5.14)
Handgrip				
	Cases	16.3 (7.83-30.57)	16.9 (10.5-24.48)	**1.17** (0.56-2.76)
	Controls	**25.75** (9.75-38.8)	15.2 (5.9-25.9)	**2.72** (1.11-4.27)

Value are expressed as median (interquartile range)

LDF results



Graphic representation of low and high frequencies after activated conditions of sympathetic ANS

Conclusion: Patients with cervical dystonia have subclinical autonomic dysfunction according to both clinical and neurophysiologic evaluation. Altered parasympathetic-sympathetic integration might be hypothesized.

Disclosure: No disclosure

EPR-109

Art Therapy for Parkinson's disease: preliminary findings from the ExplorARTPD Study

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Background and aims: Art Therapy (AT) holds therapeutic potential in different clinical populations. This study aims to determine whether AT improves motor performance and quality of life in patients with Parkinson's disease (PD).
Methods: Prospective, open-label trial exploring the effects of proctored AT on PD subjects. The AT involved a series of projects specifically addressing PD-related disabilities. Assessments were performed before and after twenty 90-minute sessions of AT and included: Activities-specific Balance Confidence Scale (ABC), Apathy Scale, Beck Anxiety Inventory, Beck Depression Inventory-II (BDI-II), Enhanced Scale for Positive Symptoms, MDS-UPDRS (all components), Modified Fatigue Impact Scale, Montreal Cognitive Assessment, Parkinson's disease Questionnaire-39, Pegboard Test, PROMIS-Self-Efficacy, Timed Up & Go (TUG-1: regular walking; TUG-2: serial subtractions; TUG-3: fast pace), and Toronto Alexithymia Scale. Specific effects of AT on visuospatial functions were assessed by computerized Navon, Visual Search, and Simple Reaction Time tests.
Results: 39 PD subjects completed the study. Following AT, significant score improvements emerged in: UPDRS-total (mean change ± standard deviation: -8.1±10.2; 2-tailed paired t-test: $p<0.0001$, UPDRS-I (-2.1±4.4; $p=0.005$), UPDRS-III (-5.0±6.8; $p<0.0001$), BDI-II (-2.8±6.4; $p=0.01$), TUG-2 (-1.9±4.2 seconds; $p=0.018$), ABC (9.3%±9.4%; $p=0.018$), Pegboard non-dominant hand (-28.0±62.4 seconds; $p=0.038$), Navon test local stimuli (-0.14±0.39 seconds; $p=0.036$) and PDQ-39 emotions (-0.9±2.7; $p=0.036$).
Conclusion: This exploratory unblinded and uncontrolled trial in PD suggests that AT may improve motor function, including manual dexterity, gait and balance, while ameliorating depressive symptoms, non-motor experiences of daily living and emotional wellbeing, as well as visuo-spatial processing. Future controlled trials including objective outcome measures such as imaging and eye movement studies are warranted.
Disclosure: The ExplorARTPD Study is supported by The Kellar Family Foundation, Grant ID # C17-00191

EPR-110

Decoupled and disengaged: Distinct functional cortico-striatal circuits underlie apathy domains in Huntington's disease

A. De Paepe [1], C. Garcia-Gorro [1], S. Martinez-Horta [1], P. Pérez [1], J. Kulisevsky [2], N. Rodriguez-Dechicha [2], I. Vaquer [2], S. Subira [2], M. Calops [3], E. Muñoz [4], P. Santacruz [4], J. Ruiz-Idiago [5], C. Mareca [6], R. De Diego-Balaguer [7], E. Camara [7]

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Background and aims: Apathy, a quantitative reduction of goal-directed behavior, is a common psychobehavioral condition in neurologic disorders such as Huntington's disease, significantly burdening daily life. A multidimensional entity, apathy has been attributed to dysfunctions in large-scale corticostriatal networks that elicit cognitive, motor, and limbic functions. Moreover, recent work indicates that disrupted connectivity, as opposed to local gray matter atrophy, may be more predictive of apathy profiles. As such, the present study investigates functional cortico-striatal circuits to parse apart the disruptions underpinning apathy domains.

Methods: 39 Huntington's disease gene-expansion carriers underwent an MRI scan and apathy evaluation using the short-Lille Apathy Rating Scale (LARS-s), decomposed into cognitive, auto-activation, and emotional domains. Seed-based functional connectivity analysis with the caudate nucleus, putamen, and nucleus accumbens bilaterally was carried out using the CONN-fMRI Functional Connectivity toolbox v1.2 (www.nitrc.org/projects/conn).

Results: Global apathy was related with reduced functional cortico-striatal connectivity across dorsal, ventral, and temporal areas. Meanwhile, cognitive, action-initiation, and emotional apathy domains corresponded with distinct patterns of cortico-striatal dysfunction. In particular, while cognitive apathy was associated with decreased connectivity between the caudate and putamen with superior frontal and temporal regions, emotional apathy involved disruptions between the nucleus accumbens and the anterior cingulate cortex. In line with past literature, auto-activation deficit was linked with both cognitive and limbic cortical territories.

Conclusion: These findings corroborate the pivotal role that disruptions in discrete cortico-striatal circuits play in the evolution of apathy as a multidimensional entity, opening the door to more individualized diagnosis and management in neurologic disorders.

Disclosure: Nothing to disclose.

EPR-111

Motor and non-motor burden in Parkinson's disease is not dependent on severity of apathy

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Background and aims: We examined clinical correlates of different severities of apathy in a cohort of 72 Parkinson's disease (PD) patients.

Methods: We recruited 72 patients through our outpatient clinic and screened for apathy using the Lille Apathy Rating Scale (LARS). Patients with a LARS score higher than -21 were considered apathetic. We defined three categories: mildly (-21 to -17), moderately (-16 to -10) and severely (-9 and above) apathetic. Non-motor burden was evaluated using the Non-Motor Symptoms Questionnaire (NMSQ) and motor symptoms with the Unified Parkinson's disease Rating Scale (MDS-UPDRS). Differences in NMSQ and MDS-UPDRS motor scores between apathy groups was determined using the non-parametric Kruskal-Wallis test.

Results: In our sample 55 patients (76.4%) were male. Mean age was 67.46±10.45 years and mean disease duration was 7.6±5.38 years. NMSQ and motor UPDRS score is higher in the apathetic versus the non-apathetic group ($p<0.001$ and $p=0.001$ respectively). We found no significant differences in age ($p=0.60$) or disease duration ($p=0.78$) between apathy groups. NMSQ and motor UPDRS scores did not differ significantly between the mildly, moderately and severely apathetic group.

Conclusion: Previous studies have noted the relation between apathy and a higher burden motor and non-motor symptoms in PD patients. We found that merely the presence of apathy is related to a higher motor and non-motor burden, independent of its clinical severity. Apathy is often overlooked, however even in its mildest form it constitutes a marker of a more severe motor and non-motor phenotype in PD patients.

Disclosure: Funding for this research was granted by the Move for Parkinson patient group.

MS and related disorders 2

EPR-112

Rituximab treatment for Multiple Sclerosis: the importance of dosing regimen

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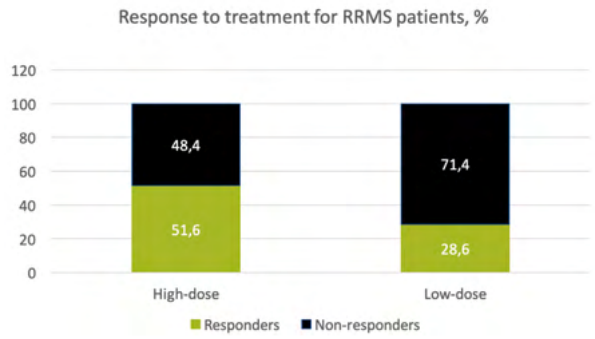
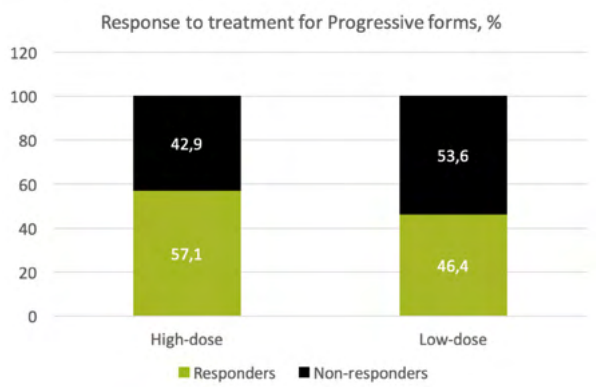
[1] Porto, Portugal, [2] Lisboa, Portugal

Background and aims: Rituximab, a monoclonal antibody anti-CD20, is used as an off-label treatment in Multiple Sclerosis (MS) with good efficacy and safety profile. Studies to improve knowledge concerning the ideal dosing regimen are needed. Our aims is to study the effectiveness and safety of rituximab in MS patients regarding treatment regimens (TR).
Methods: Retrospective observational single-center study of MS patients treated with Rituximab. Characterization of demographic and clinical data (relapses, Expanded Disability Status Scale (EDSS), annual dosing regimen and side effects). Two groups of TR were considered: high-dose regimen (1,000-1,500mg/year) and low-dose regimen (<1,000mg/year). Responders were defined by the absence of relapses and disability progression or physician perception of therapeutic benefit during follow-up period.
Results: 80 patients were included, 38 relapsing-remitting MS (RRMS) and 42 progressive forms. For RRMS patients, there was an higher percentage of responders for high-dose regimen (51,6% vs. 28,6%) with absence of disability progression (77,4% vs. 57,1%); however, fewer side-effects (14,3% vs. 29%) and higher persistence in treatment (71,4% vs. 67,7%) were observed for low-dose group. In progressive forms, percentage of responders was higher in the high-dose group (57,1% vs. 46,4%), with less progression of disability (78,6% vs. 64,3%), lower percentage of treatment discontinuation (35,7% vs. 60,7%) and side effects (28,6% vs. 60,7%).



Response to treatment for RRMS patients



Response to treatment for Progressive forms

Conclusion: In our cohort, TR with higher doses of Rituximab appeared to be more efficiently for disease's stabilization in both RRMS and progressive forms. TR with low-doses should be individualized and may be indicated according to clinical response and side effects.
Disclosure: Nothing to disclose

EPR-113

Eosinophilia in standard and extended interval natalizumab therapy

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Background and aims: Natalizumab is a potent treatment for relapsing remitting multiple sclerosis. It binds to a4 integrin receptors on the surface of leucocytes, inhibiting transmigration of T-cells across the blood brain barrier. Lymphocytosis, basophilia and eosinophilia have all been associated with the standard 4-weekly interval of natalizumab. The lymphocytosis may act as a biomarker of drug efficacy. Recent evidence suggests that extending the dosing to 6-weekly intervals is associated with comparable therapeutic benefit while lowering the risk of toxicity.
Methods: We assessed the changes in eosinophil count during standard interval dosing (SID) and extended interval dosing (EID) on all patients on natalizumab treatment. It was measured pre-treatment and every three months during therapy. We specifically evaluated changes in eosinophil count on patients transitioned from SID to EID.
Results: We recorded 92 patients on natalizumab. On SID, average pre-treatment eosinophil count was 0.158 (values expressed as x10^9/L). It increased once established on treatment and remained between 0.3 and 0.4. 10 patients transitioned from SID to EID. Pre-treatment eosinophil count averaged 0.19. Eight patients experienced at least a 0.1 rise in eosinophil count. One patient's increased by 0.2 and one patient showed no response.
Conclusion: Natalizumab induced lymphocytosis may reflect a biomarker of therapeutic efficacy. Eosinophilia could have a similar use. Our results show that eosinophilia in EID is lower than in SID. Sustained changes in biomarkers between EID and SID could support the efficacy of EID. Larger studies are needed to evaluate haematological changes with natalizumab and their use as therapeutic markers.
Disclosure: Nothing to disclose

EPR-114

Real-world smartphone keyboard interactions discriminates between different levels of disability in multiple sclerosis

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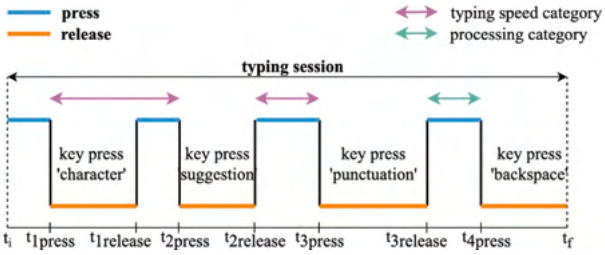
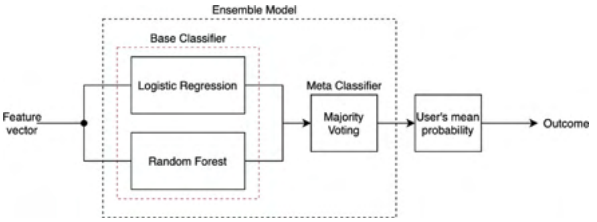
Amsterdam, The Netherlands

Background and aims: Smartphones provide the possibility to remotely monitor people with neurological conditions, including multiple sclerosis (MS). Typing requires physical and cognitive functions which are affected in people with MS (pwMS). Therefore, typing behaviour could reveal information about the clinical status. This study investigated whether smartphone collected keystroke dynamics (KD) could discriminate 1) between healthy controls (HC) and pwMS, and 2) between pwMS with different disability levels.
Methods: Two weeks of KD were aggregated per hour from 97 pwMS and 22 HC. A median split of the Expanded Disability Status Scale (EDSS) was used as a threshold between low disability levels (EDSS≤3.5) and higher levels (EDSS>3.5). An interpretable ensemble model was designed by combining both a logistic regression and a random forest to capture linear and non-linear trends between features with the highest predictive power and the outcome. The models' performances were assessed through a leave-one-subject-out cross-validation scheme.



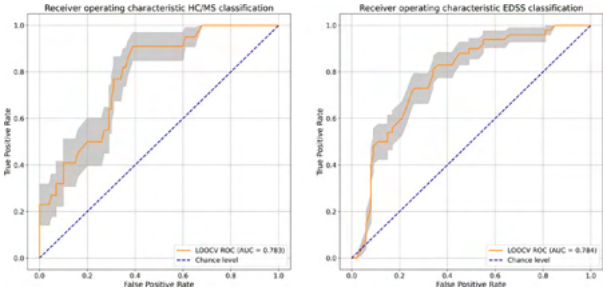
A graphical representation of a typing session. Features originate from the hold time, the release time or a combination, dependent on the type of key press.



A graphical representation of the ensemble model, consisting of both logistic regression and a random forest.

Results: The best performing model to discriminate between HC and pwMS included two typing speed features, the number of suggestions, age and gender and achieved an Area Under the Curve (AUC) of 0.79 [0.69–0.84; 95% Confidence Interval (CI)] The discrimination between

EDSS>3.5 and EDSS≤3.5, achieved an AUC=0.78 [0.69–0.88; CI] and included three typing speed features, a mental processing feature and age. Both models were primarily driven by KD.



ROC curve. Left plot: healthy controls vs people with multiple sclerosis. Right plot: EDSS greater than 3.5 vs EDSS lower or equal to 3.5.

Conclusion: Typing behaviour can distinguish between HC and pwMS and within MS between different disability levels. These findings show the potential of KD as a digital biomarker to remotely monitor the clinical status in pwMS.
Disclosure: The study received funding from Health Holland (Top Sector Life Sciences and Health), Stichting MS Research, and Biogen.

EPR-115

Assessig efficacy and safety of ocrelizumab in active relapsing multiple sclerosis: PRO-MSACTIVE study interim analysis

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Background and aims: PRO-MSACTIVE (NCT03589105) is a phase IV study evaluating the efficacy, safety and impact of ocrelizumab (OCR), an anti-CD20 antibody, on patient reported outcomes in patients with active relapsing multiple sclerosis (RMS). We report the interim analysis findings.
Methods: In PRO-MSACTIVE, patients with active RMS, ≥18 years, receive OCR infusions for a 48-weeks treatment period. The primary endpoint of the study was the percentage of patients free of disease activity at week (W) 48 (defined by no relapse since enrolment and no T1 gadolinium (Gd)-enhancing lesion and no new and/or enlarging T2 lesion as detected by brain MRI [without MRI rebaseline]) and was evaluated in this interim analysis using the population of patients who have completed the 48 weeks of treatment phase before France COVID-19 lockdown.
Results: In total, 422 patients (375 RRMS, 47 SPMS; female 73.7%; mean (SD) age 39.7 years (10.5); 25.1% naïve of previous DMT; mean (SD) baseline EDSS 2.80 (2.04)) were enrolled. This interim analysis included data from 335 patients at W48. Most patients (65.1% [95%CI 59.7%–70.2%]) were free of all protocol-defined disease activity events. Regarding individual activity events, 87.2% of patients were relapse free at W48, 83.6% had no T1 Gd-enhancing lesion and 76.1% had no new/enlarging T2 lesion. The adjusted annualised relapse rate (0.13) was low. There were no deaths and safety results were consistent with prior studies.
Conclusion: The efficacy of ocrelizumab in RMS patients was confirmed in a pragmatic setting and was in line with the other OCR study results. No safety signals were observed.
Disclosure: This research was funded by Roche SAS, France. Writing and editorial assistance for this presentation was provided by Potentiel d'Action, France, and funded by Roche SAS, France.

EPR-116

MicroRNA biomarker panel for Multiple Sclerosis: an exploratory validation study

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[1] Porto, Portugal, [2] Lisboa, Portugal, [3] Coimbra, Portugal

Background and aims: Circulating microRNAs (miRs) are appealing novel disease biomarkers due to the low cost, minimal invasiveness, and speed of the analytic process. We have already reported a panel of four circulating microRNAs, miR-1, miR-22, miR-146a and miR-155, with promising value as MS biomarker. To access the validity, specificity, and sensitivity of this miR panel as an MS diagnostic tool we we sought to analyse its diagnostic performance in different groups according to clinical features (typical vs atypical, Ms course and disease activity).
Methods: MiRs serum levels were quantified in 74 patients with definitive MS diagnosis accordingly to 2017 McDonald's Criteria (40F, six with Progressive MS, 12 with active disease, 29% HLA-DRB1*15 positive). 10 of these patients had atypical clinical symptoms with more pronounced cognitive and behavioural impairment. 42 individual without autoimmune and neurological pathologies were included in the control group.
Results: As previously described the combination of the four studied miRs had a good diagnostic ability for MS with 90% specificity and 84% sensitivity (AUC=0.95). Considering patients with atypical symptoms the diagnostic performance was maintained allowing the discrimination from controls with 95% specificity and 87% sensitivity (AUC=0.99). No differences were observed between patients with typical and atypical clinical presentation. Also, miR levels were not influenced by clinical form or disease activity, nor by HLA.DRB1*15 presence.
Conclusion: This small exploratory study support the use of the panel miR-21 – miR-22 – miR-146a – miR-155 as a reliable MS diagnostic tool. Other important MS susceptibility factors are being included in this panel.
Disclosure: Funding: BIEM. for the Epigenetics Project Investigators.

EPR-117

Ocrelizumab impact on patient-reported outcomes in active relapsing multiple sclerosis: PRO-MSACTIVE interim analysis

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Background and aims: Patient satisfaction and quality of life improvement is important to ensure persistence with treatment. In PRO-MSACTIVE (NCT03589105) phase IV study, evaluating ocrelizumab (OCR), patients with active relapsing multiple sclerosis (RMS) were administered self-reported patient reported outcomes (PROs) questionnaires. We report the interim analysis of PROs data.
Methods: In PRO-MSACTIVE, patients receive OCR infusions for a 48-weeks treatment period. Efficacy and safety were assessed and several PROs questionnaires were self-administered prior to the administration of OCR: MS symptom severity scale (SymptoMScreen), Modified Fatigue Impact Scale (MFIS), EuroQol 5-Dimension Questionnaire (EQ-5D-5L with VAS), Work Productivity and Activity Impairment scale (WPAI:SHP), Multiple Sclerosis International Quality of Life Questionnaire (MusiQoL) and Treatment Satisfaction Questionnaire (TSQM-14).
Results: PRO-MSACTIVE has enrolled 422 patients in France (female 73.7%; mean (SD) age 39.7 years (10.5); 25.1% naïve of previous DMT; mean (SD) baseline EDSS 2.80 (2.04)). This interim analysis included data at W48 from 335 patients who have completed their treatment period before COVID-19 lockdown. Improvement from baseline total mean (SD) scores were observed for SymptoMScreen (-1.3 (8.8)), MFIS (-2.9 (13.47)), EQ-5D-5L with VAS health state score (+4.07 (17.02)), WPAI:SHP activity impairment (-5.31 (23.65)), MusiQoL (+1.52 (11.0)) and TSQM-14 (+8.13 (21.39)). TSQM-14 total mean (SD) score improved from 59.7 (19.69) to 68.55 (20.03). The largest improvements from baseline were observed for MusiQoL on the psychological wellbeing, coping and activities of daily living domains. EDSS score was improved (<-0.5) or stable (-0.5; +0.5) for 85.4% of patients.
Conclusion: In PRO-MSACTIVE, patients with active RMS reported improvement in PROs from baseline to W48.
Disclosure: This research was funded by Roche SAS, France. Writing and editorial assistance for this presentation was provided by Potentiel d'Action, France, and funded by Roche SAS, France.

EPR-118

Real World Use of Natalizumab in Austria: Data from the Austrian Mulitple Sclerosis Treatment Registry (AMSTR)

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Background and aims: With the approval of Natalizumab in Europe in 2006, the Austrian Multiple Sclerosis Therapy Registry (AMSTR) was established. Based on this, over 10-year data on efficacy, safety and discontinuation could be collected.
Methods: Data retrieved from the AMSTR contained baseline characteristics, follow-up visits, drop-outs and treatment restarters as well as annualised relapse rate (ARR) and Expanded Disability Status Scale (EDSS).
Results: A total of 1,596 Natalizumab patients (71% women, n=1,133) were included in the analysis and the observed treatment duration ranged from 0–164 months (13.6 years). The ARR was 2.0 at baseline, decreasing to 0.13 after two years and 0.01 after 10 years. The median EDSS remained stable at 2.5 from baseline to last follow up (median 4.3 years). John Cunningham virus (JCV) seropositivity was the most common specified reason for treatment discontinuation (40%, n=452). Of 1,502 patients in the follow-up analysis, 1,297 (86.4%) reported no adverse events (AE). The most common AEs were infections and infusion related reactions. There were two confirmed cases of Progressive Multifocal Leukoencephalopathy (PML), two suspected cases and one death. The secondary progressive multiple sclerosis (SPMS) conversion rate was 24.8% (n=373).
Conclusion: The high efficacy of Natalizumab in patients with highly active relapsing remitting multiple sclerosis could be confirmed in our real-world cohort even after follow up of more than 10 years. Moreover, this nationwide registry study did not reveal any new safety aspects with long term use of Natalizumab.
Disclosure: There are no disclosures regarding this abstract.

Muscle and neuromuscular junction disease 1

EPR-119

Clinical and genetic spectrum of a large cohort of delta-sarcoglycan muscular dystrophy.

J. Alonso Perez [1], J. Díaz-Manera [2]
[1] *Tarragona, Spain,* [2] *Barcelona Spain*

Background and aims: Sarcoglycanopathies comprise four subtypes of autosomal recessive limb-girdle muscular dystrophies. Delta-sarcoglycanopathy (LGMDR6) is the least frequent of all sarcoglycanopaphies and it is considered an ultra-rare disease. Our aim was to characterize the clinical and genetic data of a large cohort of LGMDR6 patients and to investigate whether genetic or protein expression data could predict the severity of the disease.
Methods: We contacted 90 different neuromuscular units over the world and collected demographic, genetic, clinical and muscle biopsy features data of patients with a genetic confirmed diagnosis of LGMDR6
Results: We identified 23 patients from nine different countries. There was a history of consanguinity in 87% of the patients. Proximal muscle weakness was the most common presenting symptom. Distal muscle weakness was observed early on the progression of the disease. Cardiac involvement was observed in five patients (21.7%) and four patients (17.4%) required non-invasive ventilation. 60% of patients were wheelchair-bound since a mean of 14.65 years old. Patients with an undetectable expression of the sarcoglycan complex measure by muscle immuno-histochemistry have a significant early onset of the disease and early age of lost ambulation compared to patients with residual protein expression.
Conclusion: This study confirm that delta-sarco-glycanopathy is an ultrarare neuromuscular condition and describes the clinical and molecular data of the largest cohort of patients reported so far. Our results show LGMDR6 is a very severe and quickly progressive disease characterized by global muscle limbs weakness. There is a correlation between remaining protein expression, age at onset and disease's severity.
Disclosure: No disclosures.

EPR-120

Investigating intra-individual variability in oxidative deficiency in mitochondrial myopathy

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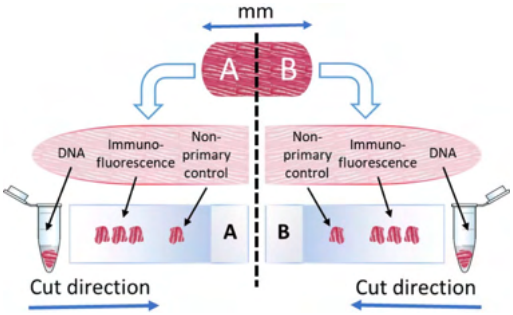
Background and aims: During and after embryogenesis, inherited pathogenic mitochondrial DNA (mtDNA) mutations can segregate, clonally expand over their dysfunction threshold or be lost from individual cells. Affected skeletal muscles accumulate oxidative deficient fibres at variable rates and spatial patterns, before developing progressive myopathy. We aim to evaluate this intra-individual variability.
Methods: Using immunofluorescence, we quantified mitochondrial proteins NDUFB8 (complex I) and MTCO1 (complex IV) in post-mortem frozen tissue blocks from quadriceps and tibialis anterior muscles of five patients harbouring the m.3243A>G mutation. Heteroplasmy will be quantified using pyrosequencing. We cut three serial sections per block, measuring and splitting bigger blocks to obtain pairs of known intermediate distance (Fig).



Example of serial sections from split tissue blocks measuring intermediate distances

Results: We analysed ~26,622 fibres from two patients (P1-2) calculating percentages of deficient fibres. Within serial sections per block, the mean difference of NDUFB8 deficiency was 12±18% (2SD) and up to 29%. Paired blocks 0.9–1.5cm apart revealed deficiency differences of 17–29%. For P1-2 respectively, variability of NDUFB8 deficiency was higher for tibialis anterior (66–28%) than quadriceps (36–17%), while mean deficiency across all sections was 43±36% (18–83% range) for P1 and 33±16% (18–46% range) for P2.
Conclusion: Confirming and characterising the determinants of this surprisingly high inter- and intra-muscular variability will help us to better understand the mechanisms underlying the observed phenotypical heterogeneity of mitochondrial myopathies. We should account for both natural and artificially introduced variability when designing protocols and outcome measures for future clinical studies.
Disclosure: This work is funded by Wellcome.

EPR-121

A stagewise response to mitochondrial dysfunction in mitochondrial DNA maintenance disorders

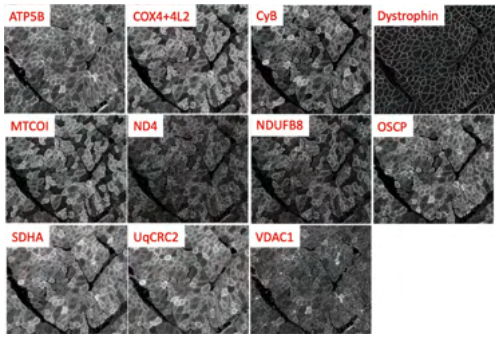
T. Bernardino Gomes [1], A. Vincent [2], C. Chen [2], K. Pabis [2], A. Reeve [2], V. Perissi [3], D. McDonald [4], A. Filby [4], D. Lehmann [5], S. Zeirz [6], R. Capaldi [7], M. Mauresch [8], A. Reeve [2], C. Lawless [2]

[1] Department of Clinical Neurology, Newcastle upon Tyne, United Kingdom, [2] Wellcome Centre for Mitochondrial Research, Newcastle upon Tyne, United Kingdom, [3] Boston University, Boston, United States, [4] FCCF, Newcastle University, Newcastle upon Tyne, United Kingdom, [5] Ulm University, Ulm, Germany, [6] Martin Luther University Halle-Wittenberg, Halle, Germany, [7] Cell State Biosciences, Tucson, United States, [8] Oregon, United States

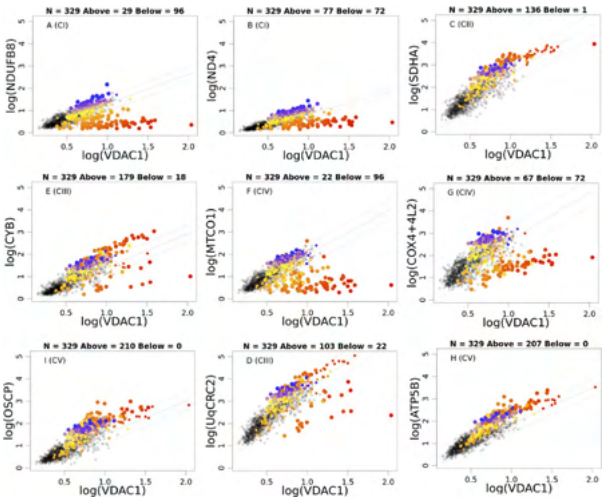
Background and aims: Mitochondrial DNA (mtDNA) deletions clonally expand in skeletal muscle of patients with mtDNA maintenance disorders causing mitochondrial oxidative phosphorylation dysfunction. Previously we found these deletions arising and accumulating in perinuclear mitochondria, alongside changes in retrograde stress signalling and mitochondrial biogenesis, before spreading throughout the muscle fibre. The current study investigates deficiency of all mitochondrial complexes and assesses key signalling pathways, all simultaneously on the same tissue section, to investigate if the cellular response to mitochondrial dysfunction is stagewise.

Methods: We use imaging mass cytometry in a cohort of mtDNA maintenance disorders (POLG n=8, TWNK n=3, RRM2B n=1) to simultaneously quantify levels of mitochondrial complexes I-IV, ATP synthase, and a comprehensive list of key cellular signalling proteins, alongside a mitochondrial mass marker (VDAC1).

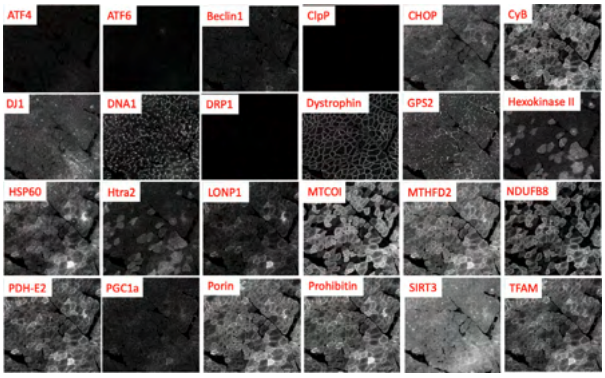
Results: Complexes I and IV were the most commonly deficient, with a smaller proportion of complex III and ATP synthase deficient fibres. Interestingly, in fibres deficient for at least one complex, all unaffected complexes were commonly upregulated beyond the expected increase in mitochondrial mass in ragged-red fibres. We also found that respiratory chain deficient fibres have an increased abundance of proteins involved in the mitochondrial unfolded protein response and mitochondrial protein synthesis.



Mitochondrial proteins imaging mass cytometry in skeletal muscle: complex I (NDUFB8, ND4), II (SDHA), III (CyB, UqCRC2), IV (MTCO1, COX4+4L2), ATP synthase (OSCP, ATP5B), and mitochondrial mass (VDAC1) and muscle membrane (dystrophin) markers.



2D plots of mitochondrial proteins against mitochondrial mass (VDAC1). Control 95% predictive interval plotted as dashed line with fibres (points) bellow the interval classified as deficient and coloured red based on NDUFB8 levels. Control fibres in grey.



Unfolded protein response: ClpP, CHOP, HSP60, Htra2; stress response: ATF4/6, GPS2, Sirt3; mitophagy: beclin1; proteostasis: DJ1, LONP1, prohibitin; fission: DRP1; biogenesis: PGC1a, TFAM; one carbon cycle: MTHFD2; and glycolysis: PDH-E2, Hexokinase II.

Conclusion: Our work profiles all five oxidative phosphorylation complexes in mtDNA maintenance disorders for the first time at the single fibre level. Furthermore, our analysis suggests the cellular response to mitochondrial dysfunction is stagewise. Further analysis is required to understand if there are differences in signalling response depending on the mitochondrial complexes that are deficient.

Disclosure: This work is funded by Wellcome.

EPR-122

Simultaneous isolation of fibroadipogenic progenitors and satellite cells from frozen human muscle explants

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Background and aims: Skeletal muscle comprises multiple cell types including satellite-cells (SC) and fibroadipogenic precursor cells (FAPs) involved in degeneration process in muscular dystrophies(MDs). A characterization of the interaction between both cell types in human samples has not been performed due to the lack of availability of fresh muscles to isolate these cells from MD patients. We developed a new protocol to isolate SC and FAPs from frozen explants obtained from muscle biopsies of healthy volunteers or MD patients for further analysis in vitro.

Methods: We usually freeze small portions of each muscle biopsy obtained for diagnosis in freezing medium at our laboratory. We thawed and cultured muscle explants from healthy controls and one DMD patient in growth culture medium and characterise the cells as described in results section.

Results: Flow-cytometry and immunofluorescence showed that cells sprouting from explants expressed CD56 (marker of SC) or PDGF-receptor-alpha (marker of FAPs). We isolated these cells using sorting for further in vitro characterization. Isolated SC differentiated to myotubes while FAPs differentiated to adipocytes when cultured in adipogenic medium, or to fibrocytes expressing collagen-I when cultured with TGF-beta. Immortalized FAPs (iFAPs) maintained intact their ability to differentiate to adipocyte or to fibrocyte.

Conclusion: This new protocol allows the obtention of SC and FAPs from muscle biopsies of the same patient stored in sample collections that will enable to increase our knowledge in the skeletal muscle degenerative process taking place in neuromuscular diseases. IFAPs could be used in high-throughput drug screening protocols to identify compounds blocking their fibroadipogenic differentiation.

Disclosure: Authors have no relevant disclosures

EPR-123

Longer-term Safety Data in Individuals with Later-onset SMA Support the Favourable Tolerability Profile of Nusinersen

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Background and aims: Nusinersen has a favourable benefit-risk profile in later-onset SMA demonstrated by a previous integrated safety analysis. We aimed to provide additional information by assessing adverse events (AEs) associated with lumbar puncture (LP) using longer-term SHINE data.

Methods: SHINE (NCT02594124) is an ongoing, open-label extension study. Safety data for participants with later-onset SMA were assessed from nusinersen initiation in CS1, CS2, EMBRACE, CHERISH and/or SHINE to SHINE 27 August 2019 data cut.

Results: Median time of observation and age at nusinersen initiation were 4.0 (range: 0.08–7.6) and 4.5 (1.4–16.0) years. The Medical Dictionary for Regulatory Activities preferred term post-LP syndrome was reported in 13% (24/190) of participants in Year 1, and 6–23% across Years two to seven (n=182 to 35). The majority of cases were mild/moderate. Serious post-LP syndrome was reported in 2% (3/190) of participants in Year 1, and 3% in each subsequent year. The incidence of headache generally decreased over time from 26% (50/190) in Year one to 10–17% in the subsequent six years. Vomiting occurred in 20% (38/190) in Year one and 7–14% in subsequent years. There were no serious events of headache or vomiting and most cases were mild. No cases of meningitis or hydrocephalus were reported.

Conclusion: The incidence of AEs typically associated with LP appears to decrease/stabilize over time in individuals with later-onset SMA. Most events were mild/moderate and the incidence of serious AEs was low. These longer-term data from SHINE support the favourable benefit-risk and tolerability profile of nusinersen.

Disclosure: This study was sponsored by Biogen (Cambridge, MA, USA). Writing and editorial support for the preparation of this abstract was provided by Excel Scientific Solutions (Horsham, UK): funding was provided by Biogen.

EPR-124

Diagnosis of DOK7 Congenital Myasthenic Syndrome during pregnancy

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Background and aims: Pregnancy among patients with congenital myasthenic syndrome (CMS) is a rare occurrence, and clinical outcome is debatable and considered unpredictable. Since most of the patients with CMS reach adulthood, questions regarding clinical outcome with pregnancy arise.
Methods: N/A
Results: We describe a 38-year-old Portuguese female who presented in the second trimester of pregnancy with proximal fluctuating limb-girdle weakness, hyperlordosis, waddling gait, dysphagia, dysphonia and ptosis, with no ophthalmoparesis. Initial diagnosis of seronegative myasthenia, supported by neurophysiology findings, led to unsuccessful treatment with intravenous immunoglobulin, pyridostigmine, prednisolone and plasmapheresis, and the patient slowly progressed to a severe tetraparesis with facial and bulbar involvement. Given the incomplete response to immunotherapy and the clinical features of a limb-girdle pattern of weakness, waddling gait, hyperlordosis and no ophthalmoparesis, genetic testing for CMS was requested and identified a novel compound heterozygous mutation (c.1124_1127dupTGCC and c.935_936del) in the DOK7 gene. Subsequent treatment with salbutamol resulted in substantial clinical benefit.
Conclusion: This case underlines the importance of considering the diagnosis of CMS in patients with fluctuating weakness during pregnancy. We performed a literature review regarding pregnancy and CMS, particularly due to DOK7 mutations, and based on our observations, pregnancy might be a risk factor for clinical onset or worsening of symptoms in DOK7 CMS patients. We recommend that patients of child-bearing potential diagnosed with CMS, particularly due to DOK7 mutations, should be counseled in advance and closely followed during pregnancy and postpartum period, through a multidisciplinary approach for optimal clinical control and avoid maternal and fetal adverse outcomes.
Disclosure: Nothing to disclose.

EPR-125

Time-course and predictors of outcome in myasthenic crisis: longitudinal 20 years experience from a Neuromuscular clinic

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Background and aims: Aim of the study is to determine demographic characteristics, clinical features, treatment regimens and outcome of myasthenic crisis (MC) in a myasthenic population.
Methods: The retrospective study included patients of our Neuromuscular Center who presented a MC between 2000 and 2020 and with a minimum follow up of 12 months. We collected demographic, clinical, laboratory and treatment features. Primary outcomes were risk of intubation and duration of ICU stay.
Results: 90 patients were enrolled in the study, 53 females (58.8%) and 37 males (41.1%). Median age at diagnosis was 59 (range 16–88) and median age at MC was 65 (16–88). Cases were classified as early (EOMG, 35%) or late (LOMG, 65%) onset. The time between onset of disease and MC ranged from 12 to 576 months. According to antibody profile, 78 patients (85%) presented anti-AChR antibodies, three patients (3.3%) anti-MuSK antibodies and the remaining (11%) were seronegative. 50% of the patient underwent thymectomy during overall follow up. The most common comorbidities were cardiovascular diseases (44%). The treatment of MC included plasmaexchange (26%), intravenous immunoglobulin (46%) or both (28%). 35 patients (39%) needed mechanical ventilation, including 21 males (60%) and 14 females. Male sex (p=0.002) and LOMG (p=0.0001) were predictors of intubation. Antibody titer and thymectomy did not significantly affect outcome. The mortality for MC was 5,5%, associated with multiorgan failure and comorbidities.
Conclusion: Predictors of MC outcome remained comparable to previous reports, despite higher age and high disease burden in our study.
Disclosure: The authors have no conflicts of interest

EPR-126

Micro-dystrophin gene delivery for Duchenne Muscular Dystrophy: a double-blind, randomized placebo-controlled trial

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Background and aims: Adeno-associated virus (AAV-mediated gene transfer has shown potential as a therapy to treat Duchenne Muscular Dystrophy (DMD). We developed an AAV virus vector (rAAVrh74) containing a human micro-dystrophin transgene driven by a muscle-specific promoter with a cardiac enhancer, MHCK7 (rAAVrh74. MHCK7.micro-dystrophin; SRP-9001) in order to achieve targeted expression of a shortened, functional micro-dystrophin protein in skeletal and cardiac muscle.

Methods: This 3-part study evaluates safety and efficacy of intravenous (IV) SRP-9001 in patients with DMD (NCT03769116): two 48-week randomised, double-blind, placebo-controlled periods (Parts 1 and 2) and an open-label follow-up of up to 212 weeks (Part 3). Key eligibility criteria included ambulatory boys aged four to seven years with a confirmed DMD mutation (exons 18–58), an established clinical diagnosis and stable steroid dosing (≥12 weeks). The target dose in Study 102 for the treatment group was 1.33x10^14 vg/kg (linear qPCR, supercoiled plasmid standard equivalent of 2x10^14 vg/kg), same dose previously used in Study 101. Safety endpoints included incidence of serious and treatment-emergent adverse events (up to Week 260). Primary efficacy endpoints included change in micro-dystrophin expression (baseline to Week 12) and change in North Star Ambulatory Assessment score (baseline to Week 48). Secondary endpoints included Time to Rise, 4-Stair Climb, and timed function tests (baseline to Week 48).

Results: Here we present results from the 41 patients that have been randomised and dosed to SRP-9001 or placebo in Part 1.

Conclusion: Initial safety and efficacy findings suggest the potential of SRP-9001 therapy for clinically meaningful functional improvements in people with DMD.

Disclosure: This study was funded by Sarepta Therapeutics, Inc. USA. Writing and editorial assistance was provided by MediTech Media UK, in accordance with GPP3 guidelines and funded by F. Hoffmann-La Roche Ltd, Switzerland and Sarepta Therapeutics.

COVID-19 2

EPR-127

Impact of Covid-19 pandemic on quality of life and cognitive decline in mild cognitive impairment and dementia

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Background and aims: Long-term isolation during Covid-19 pandemic seems to trigger or worsen comorbid depression and anxiety in patients with cognitive impairment; the impact on cognitive decline is less certain. We aimed to assess the effect of the coronavirus outbreak on life-quality and cognition in patients with mild cognitive impairment (MCI) and Alzheimer's disease (AD).
Methods: We included 46 patients (16 MCI and 30 AD), diagnosed according to the most recent international criteria and who underwent thorough neurological, imaging, neuropsychological and biochemical evaluation (CSF-biomarkers). The Portuguese-validated version of The Quality of Life in AD questionnaire (QoL-AD;higher scores indicating better quality of life) was applied to both patient (self-rated) and caregiver (proxy-rated). The caregiver also completed a modified version of the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE;1–2 better, three unchanged and 4–5 worse), with January/2020 as reference timepoint.
Results: Our sample had a mean-age of 69.78.9 years with a slight male prevalence (32/55,52.3%); 21/37 CSF-biomarkers suggested amyloid pathology; 19/40 had at least one ApoE4-allele. Mean self-rated QoL-AD was 32.06.5 (n=38) and proxy-rated QoL-AD 28.65.3 (n=39), with memory being the lowest scored domain overall. Mean IQCODE was 3.60.6.
Conclusion: In our cohort, proxy-rated was lower than self-rated QoL-AD; IQCODE scores pointed towards a moderate cognitive decline in the previous year. Although a potential influence of the caregiver's burden cannot be ruled out, these findings suggest that lockdown measures amid Covid-19 pandemic play a negative role both on quality-of-life and overall cognitive function in patients within the AD spectrum.
Disclosure: Nothing to disclose.

EPR-128

COVID-19 outbreak in a cognitive and behavioral care unit: specific challenges in a doubly vulnerable population

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Background and aims: Older adults constitute the most vulnerable group to SARS-CoV-2 infection, with high mortality rates. Cognitive impairement is a frequent comorbidity in this population. Neverthless, the specificities of COVID-19 in these patients remain poorly characterized. This study aims at describing the clinical characteristics and the outcome of COVID19 in patients admitted in a COVID-19 cognitive and behavioral care unit.
Methods: This is an observational prospective study conducted in the cognitive and behavioral unit of Leopold Bellan hospital in Paris. Patients with cognitive impairement for whom a confirmed diagnosis of SARS COV2 infection (PCR or Chest CT) was made were systematically included. The demographic data, clinical, laboratory and imaging findings were collected throughout hospitalization.
Results: 36 patients (median age 86, 62-98) were included. SARS COV2 infection wasn't the sole hospitalization motive. Most frequent symptoms were fatigue and fever, confusion and falls. The reported complications were depression (42%), acute respiratory distress syndrom (28%), stroke (4 patients), psychosis (4 patients), seizure (3 patients) and agitation (2 patients). In-hospital mortality was 27,8% secondary to respiratory complications. Persistant behavioral disturbance with ward wandering was observed for 41,7% of patients.
Conclusion: The prevalence of neuropsychiatric events at the acute phase of COVID-19 in our cohort was significant. Cognitive impairement and wandering were a challenge in the care of these patients. Consent for research and trial inclusions raised ethical questions. Older adults suffering from cognitive impairement and contracting SARS-CoV-2 present a double therapeutic challenge: COVID-19 and cognitive and behavioral disturbances related to their disease and to the sanitary measures.
Disclosure: No conflict of interest

EPR-129

Neurological disorders in Post-COVID patients

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Background and aims: The aim of the study is to identify the features of the lesions of the central nervous system in patients who have undergone coronavirus disease COVID-19. We examined 42 patients aged 32 to 54 years old after two to four months from the onset of COVID-19. In 20 patients, the infection was severe, in 11 patients was moderate, in 11 ones was in a mild form. There were no neurological disorders and vascular risk factors in these patients before COVID-19.
Methods: Clinical and neurological, psychodiagnostic scales (MoCa MF1-20, HADS), neuroimaging, biochemical, statistical
Results: : In 95.2% of patients, neurocognitive impairments of various severity were revealed (the mean MoCA score was 22.01±0.22 points). All patients had asthenic syndrome, increased fatigue (the average score MF1-20 was 13.0 (12.5–14.0) points). The patients had anxiety-depressive symptoms according to the HADS (pathological anxiety 9.11±1.43; depression – 6.71±1.55). Vestibular disorders were in 59.2%, cephalgic syndrome in 50%, hyposmia in 19% of patients. During 1–2 months after the onset of the viral infection five patients had ischemic strokes confirmed by neuroimaging. Of these, four patients had several ischemic nidi in the basal ganglia, neo cortex, in one patient stroke was caused by occlusion of a large vessel. In six patients, TIA in the carotid basin was registered.
Conclusion: A frequent manifestation of the post-Covid syndrome is neurological disorders in the form of cognitive impairments, asthenic, anxiety-depressive syndromes, increased fatigue, ischemic strokes and TIA.
Disclosure: No

EPR-130

The Neurological Spectrum of COVID-19 infection in hospitalized versus outpatient care

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Background and aims: Neurological symptoms are reported in over 30% of COVID-19 hospitalized patients. However, systematic studies reporting these manifestations in ambulatory patients are still missing. We aim to characterize and compare neurological phenotypes in hospitalized and ambulatory COVID-19 patients.
Methods: Retrospective study in patients with laboratory confirmation of SARS-CoV-2 infection in a tertiary hospital in the North of Portugal, between March 1st and April 30th. Data from hospitalized patients was collected through electronic medical records; ambulatory patients' data was collected using a structured telephonic survey.
Results: From a total of 283 patients hospitalized in this period with COVID-19, 116 (40.9%) had at least one neurological manifestation. Mean age was 64 years (20–100) and 58.6% were women (n=68). The most frequent manifestation was headache (24.7%), followed by myalgia (15.5%) and hyposmia (10.6%). Other neurological manifestations were reported in <10%. In this period, from 488 ambulatory patients infected with COVID-19, all but one reported at least one neurological manifestation (n=487). Mean age was 50.3 years (18–93) and 63% were women (n=307). Myalgia was the most frequent symptom (71.1%), followed by anosmia (65.4%), disgeusia (62.9%) and headache (58.4%). EPR302 Sleep disorders and cognitive complaints were also frequent (39.9% and 17.4%). Hypertension, diabetes, cardiovascular, lung and kidney disease were more prevalent in hospitalized patients.
Conclusion: In the 1st systematic evaluation of neurological symptoms in outpatient COVID-19 patients we found an extremely high rate of neurological manifestations, suggesting neurological involvement is not dependent on COVID-19 disease severity. Host susceptibility and viral characteristics may drive the neurological phenotype.
Disclosure: This work was partially funded by "Fundação para a Ciência e Tecnologia", Grant nº229 (RESEARCH4 COVID-19). No conflicts of interest to report.

EPR-131

Prevalence of neurological post-COVID-19 manifestations

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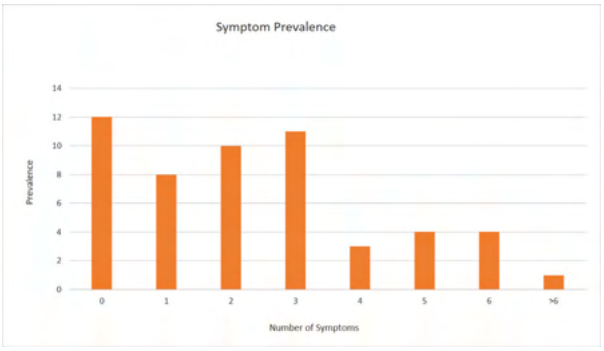
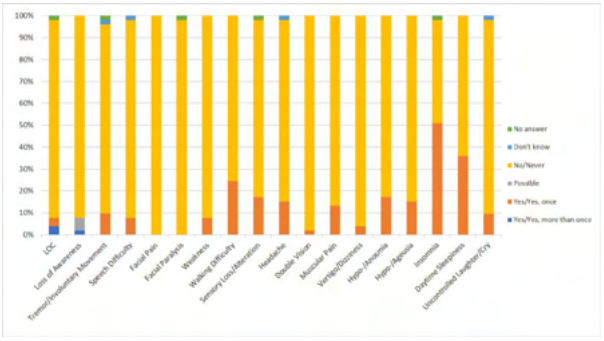
Background and aims: Although COVID-19 infection predominantly manifests with respiratory symptoms, recent studies have also reported the occurrence of neurological involvement in the acute phase as well as in the follow-up of recovered subjects

Methods: Our study focuses on assessing the prevalence of neurological sequelae in COVID-19 patients hospitalized at Ospedale Maggiore Policlinico in Milan. Seventy-five COVID-19 recovered subjects followed a general follow-up protocol including pneumological, infectious and cardiovascular assessment 5–10 months after the onset of SARS-CoV2 infection; among them, a subset of 53 patients was evaluated through a self-administered 18-item questionnaire developed ad-hoc addressing sensory, motor and cognitive neurological symptoms.

Results: Collected data has shown that 77.4% patients developed at least one neurological sequela, and 46.3% presented with more than three symptoms. Among symptomatic patients, the most prevalent manifestations were insomnia (65.9%) and daytime sleepiness (46.3%), followed by walking difficulties (31.7%). Other less frequent symptoms were headache (15.1%), hyposmia and hypogeusia (15.1%), and tremor (9.4%).



Prevalence of symptoms



18-item questionnare showing the distribution of neurological manifestations

Conclusion: Post-COVID-19 manifestations are reported in about 90% of recovered patients. This preliminary study suggests that neurological findings represent a significant part of such manifestations. We are currently expanding the questionnaire to a larger cohort of patients and correlating our findings with patients' demographical and clinical features, as well as with the severity of the previous SARS-CoV2 infection. Currently, the same questionnaire is also being validated and administered to age- and sex-matched healthy controls who have not developed symptoms suggestive of Covid-19, and a cohort of non-COVID-19 hospitalized patients.

Disclosure: No disclosures.

EPR-132

Impact of COVID-19 on care of patients treated with oral cladribine or fingolimod in CLARION – analysis of German data

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Background and aims: The COVID-19 pandemic may affect the care of patients with multiple sclerosis (PwMS). As part of the CLARION study (EUPAS24484), we describe visit distribution, compliance with cladribine tablets dosing before and during the pandemic, and COVID-19 cases.
Methods: A cohort of PwMS enrolled in CLARION German sites between SEP2018-OCT2020, and newly initiating treatment with cladribine tablets or fingolimod, were included. Those receiving fingolimod prior to cladribine initiation or vice-versa were excluded by protocol. Subgroups were defined based on enrolment dates relative to the German pandemic start date (01MAR2020).
Results: A total of 337 PwMS were included (cladribine: n=183[54.3%]; fingolimod: n=154[45.7%]). Overall, the number of baseline visits per month was 22 pre-pandemic, ranging from 11 to 14 during the spring 2020 lockdown (15MAR-15MAY) and increasing thereafter. Among those with a follow-up visit (n=194), mean (±standard deviation) time to first follow-up visit before and during the pandemic was: 178±49.0(n=61) and 180±68.1 days(n=36) for cladribine; and 150±55.7(n=56) and 191±49.2 days(n=41) for fingolimod. Median time to completion of 1st course of cladribine tablets (interquartile range) was 32.5(3.0) days before (n=108) and 33.0(3.8) days during the pandemic (n=16). Only one case of mild COVID-19 was recorded in the cladribine cohort, with onset 14 months after last dose.
Conclusion: Fewer enrolments were observed during the spring 2020 lockdown. Delays in the 1st follow-up visit occurred during the pandemic in the fingolimod cohort. For cladribine, COVID-19 had no effect on time to complete first course and only one mild case of COVID-19 was reported.
Disclosure: The study was sponsored by Merck KGaA, Darmstadt, Germany.

EPR-133

The impact of COVID-19 on clinical outcomes of people with Parkinson's disease or parkinsonism: a cohort study

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Background and aims: The COVID-19 pandemic may have hampered the management of patients with Parkinson's disease (PD) and Parkinsonian syndromes (PS). Since during the 1st epidemic bout (March-May 2020) the Local Healthcare Trust of Bologna (population=800,000) reduced scheduled healthcare activities, we designed a cohort study to assess the potential worsening of health status in PD/PS.
Methods: Design/population: clinically confirmed PD/PS recruited through a record linkage system (ParkLink cohort); matched population control cohort (ratio=1:10). Outcomes: healthcare supply measures (outpatient visits, medical tests, pre-scheduled hospital admissions); clinical outcomes (urgent hospital admissions, disease-specific hospital admissions), March-August time frames in 2019/2020. Statistical analysis: ratios of monthly rates (RR).
Results: Compared to 2019, in the ParkLink cohort (n=880, PD=696/PS=184) the overall 2020 scheduled healthcare provision was reduced ($p<0.01$), namely: any outpatient visit RR 0.67, neurologic visits 0.72, physical therapy 0.47, any medical test 0.69, pre-scheduled hospital admission 0.80. The control cohort (n=8,817) showed a similar reduction. Undesirable clinical outcomes (Figure) increased in the ParkLink cohort ($p<0.05$): urgent hospital admissions RR 1.35, major injuries 1.83, infections 3.5, acute vascular events 2.2. Conversely, the control cohort did not show any increase.

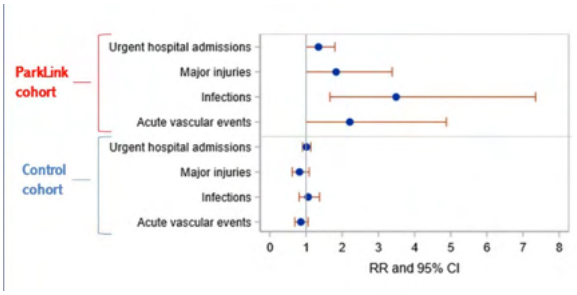

Figure. Clinical outcomes comparing March-August time frames of 2020 and 2019: ratios of average monthly rates (RR) in the ParkLink cohort and in the Control cohort.

Conclusion: During the first six months of the COVID-19 epidemic healthcare provision was substantially reduced. PD/PS patients showed a significantly higher risk of major clinical events, that was not observed in a control population. The abrupt rearrangement of healthcare supplies, as well as the general reduction of physical activity during the lockdown period, may have favoured complications in PD/PS patients.
Disclosure: Nothing to disclose

Ageing and dementia 3

EPR-134

fMRI characteristics of Medication-Overuse Headache patients

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Background and aims: Medication-overuse headache (MOH) is a secondary form of headache, and it's believed that the behaviour of MOH patients is similar to addiction. Functional magnetic resonance imaging (fMRI) studies allow to objectify pathophysiology of this phenomena. We aimed to evaluate how pain and reward systems interact with each other in MOH patients compared to chronic migraine patients through functional connectivity (FC) abnormalities.

Methods: 25 patients with chronic migraine (CM), 14 from whom with MOH history, underwent resting-state fMRI scanning during the interictal phase. Test battery: Leeds Dependence Questionnaire (LDQ), Migraine Disability Assessment Questionnaire, and Numeric Rating Scale for pain. We used "CONN functional connectivity toolbox vers.19c" to perform whole-brain seed-to-voxel and ROI-to-ROI analyses based on a two-sample t-test with pFDR-correction. Regression analysis was used for evaluating the correlation between connectivity and scale values with pFDR-correction.

Results: Demographic and clinical data summarized in Table 1 FC alterations summarized in Figure 1. Increased FC (red arrows): Nucleus Accumbens-Frontal Lobe; Nucleus Accumbens-SensoriMotor Cortex; Amygdala-Occipital Cortex; SensoriMotor Cortex-Frontal Lobe; SensoriMotor Cortex-Occipital Cortex. Decreased FC (navy arrows): Anterior Insula-Frontal Lobe; Anterior Insula-SensoriMotor Cortex. Regression analysis showed a positive correlation between all of the functional connectivity alterations and results of the LDQ, that summirized in Figure 2; The crucial score on LDQ was 12; Other scales and questionnaires didn't correlate with connectivity alterations.

	Chronic Migraine (n=11)	MOH (n=14)
Sex, female (%)	10 (91%)	12 (86%)
Age, years	32,13±7,83	36,56±9,24
Disease duration, years	12,39±8,40	15,39±9,17
Family history of migraine (%)	5 (45%)	8 (57%)
Numeric rating Scale for pain	7,06±1,34	8,21±2,66
Migraine Disability Assessment Questionnaire	49,54±32,11	56,35±43,93
Leeds Dependence Questionnaire	8,96±5,18	15,24±6,68
Hospital Anxiety and Depression Scale (anxiety)	4,65±2,40	6,24±3,32
Hospital Anxiety and Depression Scale (depression)	6,65±3,67	6,89±4,04

Table 1. Demographic and clinical data

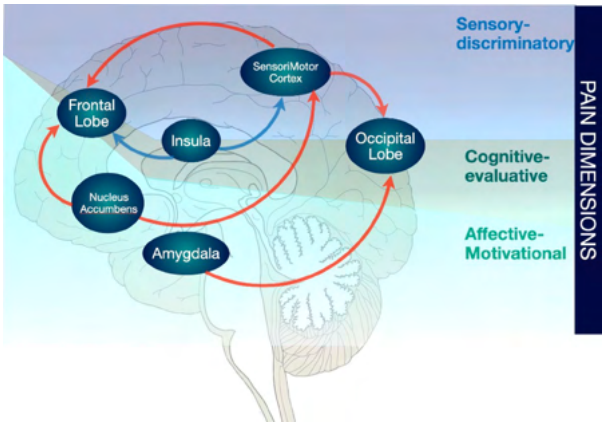

Figure 1. Schematic representation of FC alterations

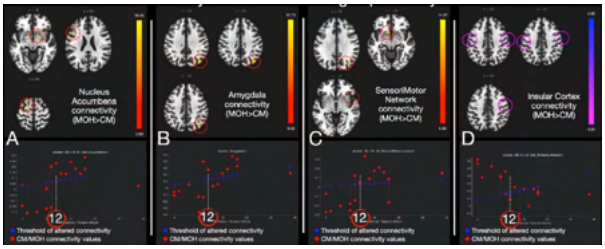

Figure 2. Association of altered FC and drug dependency.

Conclusion: 1. Functional connectivity objectify patho-physiologic mechanisms of MOH; 2. In MOH patients, the affective-motivational dimension of pain prevails over sensory-discriminative and cognitive-evaluative; 3. Leeds Dependence Questionnaire may be used as a screening instrument to determine MOH patients throw chronic migraine.

Disclosure: All authors have no relevant financial or nonfinancial relationships to disclose.

EPR-135

HTT gene CAG repeat length influence cognitive functions in subjective cognitive decline and mild cognitive impairment

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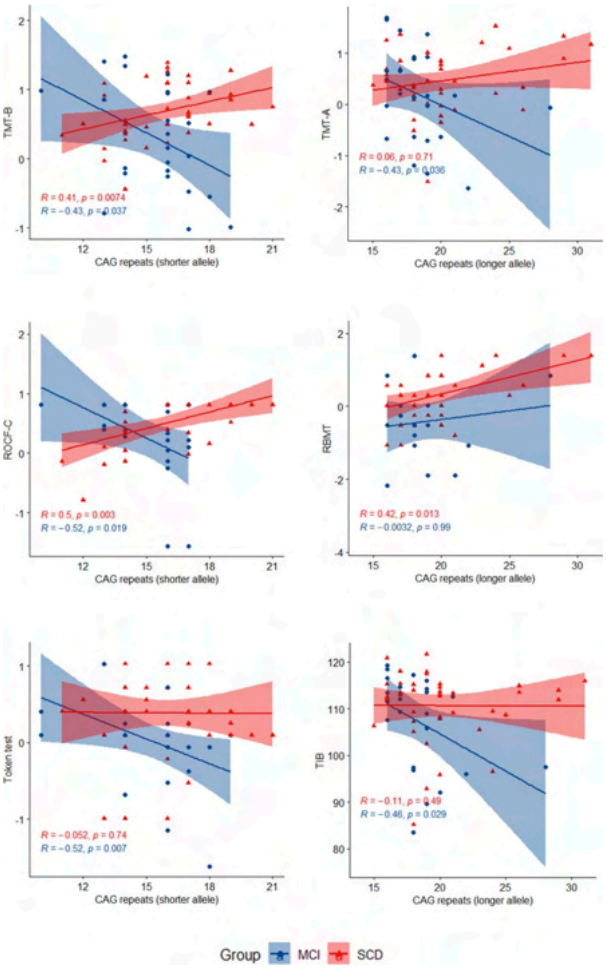
Background and aims: HTT is a gene containing a key region of CAG repeats. When expanded beyond 39 repeats, Huntington disease (HD) develops. Individuals with 36 to 39 repeats are categorized as carriers of HD alleles, whereas those with less than 35 repeats are not associated with HD. Increasing evidence suggested that CAG repeats play a role in modulating brain development and brain function. However, very few studies investigated the effect of CAG repeats in the non-pathological range on cognitive performances in non-demented individuals. In this study we aimed to test how CAG repeat length influences neuropsychological scores in patients with subjective cognitive decline (SCD) and mild cognitive impairment (MCI).
Methods: We included 75 patients (46 SCD and 29 MCI). All patients underwent an extensive neuropsychological battery and analysis of HTT alleles to quantify the number of CAG repeats.
Results: CAG repeat number was positively correlated with scores of tests assessing for executive function, visual-spatial ability and long-term memory in SCD patients while it was inversely correlated with scores of visual-spatial ability and premorbid intelligence in MCI patients. These relationships still remained also when adjusted for possible confounding factors trought multiple regression analysis. Interestingly, logarithmic models better described the associations between CAG repeats and neuropsychological scores.



Correlations between CAG repeat length and neuropsychological scores

Conclusion: CAG repeats in the HTT gene within the non-pathological range influence neuropsychological performances depending on global cognitive status. The logarithmic model suggests that the positive effect of CAG repeats in SCD patients decreases as the number of repeats grows.
Disclosure: The authors declare that they have no conflict of interest.

EPR-136

Medical treatment of epilepsy in patients with dementia – a systematic review

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Background and aims: Patients with dementia have an increased risk of developing epilepsy. When selecting anti-epileptic medication, side effects such as drowsiness and worsening of cognition should be considered. The current systematic review investigates the efficacy, tolerability, and changes in cognitive abilities after administration of anti-epileptic medication in patients with dementia and epilepsy.
Methods: We searched six databases including MEDLINE and CENTRAL, checked reference lists, contacted experts and searched Google scholar, to identify studies reporting randomized trials. Studies identified were independently screened, data extracted, and quality appraised by two researchers.
Results: One study 95 patients with Alzheimer's disease randomized to either levetiracetam, lamotrigine, or phenobarbital was included. No significant difference in efficacy was found between the different treatments, while an improvement in mini-mental state examination score and fewer adverse events were found in patients receiving levetiracetam.
Conclusion: High-quality evidence in the form of randomized trials to guide clinicians in choosing an AED in patients with dementia and concomitant epilepsy remain scarce. Levetiracetam has previously shown to possibly improve cognition in patients with both mild cognitive impairment and Alzheimer's disease and is better tolerated in the elderly population.
Disclosure: Nothing to disclose.

EPR-137

Spatial navigation and scene exploration in biomarker-defined early Alzheimer's disease

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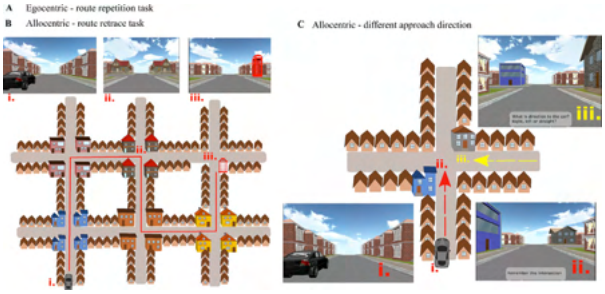
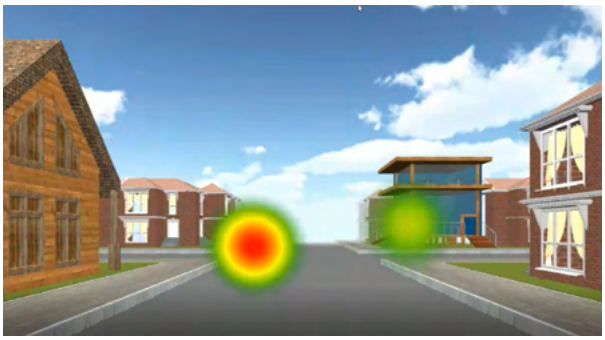
Background and aims: Spatial navigation deficits are typical for early Alzheimer´s disease (AD). Individuals with AD have altered scene exploration during navigation. We evaluated potential of a virtual spatial navigation task and scene exploration assessment to differentiate individuals with early AD from those with cognitive deficit of other etiology.
Methods: 59 participants: amnestic mild cognitive impairment (aMCI) with positive (aMCI+, n=22) and negative (aMCI AD-, n=15) AD-biomarkers and cognitively normal older adults (CN, n=22) underwent cognitive evaluation, MRI brain scan, biomarker assessment and spatial navigation testing in a virtual realistic-looking "Intersections" test. Test consisted of three tasks: i) egocentric "route repetition", where participants repeated the route through a virtual city, ii) allocentric "route retracing", where participants indicated their way back, and iii) allocentric "different approach direction" with eye-tracking, where participants indicated their positions from different perspectives at each intersection with two same and two unique houses with analysis of eye fixations of the unique houses.



"Intersections" spatial navigation test



Eye tracking example

Results: In the "route repetition" and "different approach direction" tasks, the aMCI+ group scored lower compared to the CN ($p<0.001$) and aMCI AD- ($p<0.024$) groups. In the "route retrace" task, the aMCI+ group scored lower than the CN group ($p<0.001$) but similar to the aMCI- group. Duration and number of fixations of unique landmarks was similar across all groups regardless of the task performance in the "different approach direction" task ($p>0.05$).
Conclusion: Egocentric and allocentric tasks detected spatial navigation impairment typical for early AD. Spatial navigation unlike scene exploration can differentiate aMCI individuals with AD from those with non-AD etiology.
Disclosure: National Program of Sustainability II, project no. LQ1605 (MEYS CR); the European Regional Development Fund - Project ENOCH (No. CZ.02.1.01/0.0/0.0/16_019/0000868); the Ministry of Health, Czech Republic—conceptual

EPR-138

Neuroretina thinning in Alzheimer's disease is faster and correlates with cognitive worsening and plasma neurofilaments

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Background and aims: Developing disease modifying drugs against Alzheimer's disease (AD) requires reliable markers to objectively monitor the response to treatment. Retina represents a CNS tissue easily accessible for direct and non-invasive imaging through Optical Coherence Tomography (OCT). Here, we assessed neuro-retina morphology modifications over time in a sample of Alzheimer's disease (AD), Mild Cognitive Impairment (MCI) and cognitively unimpaired participants (HC) and searched for any correlations with cognitive worsening over time.
Methods: 77 consecutive subjects (23 HC, 28 MCI and 26 AD) underwent OCT with measurement of peripapillary Retinal Nerve Fiber Layer (p-RNFL) thickness at baseline and at a mean follow up time of two (±1.32) years. Generalized estimating equation models were adopted to account for age, sex, education, baseline OCT values and within patient inter-eye dependencies
Results: AD patients showed threefold faster yearly RNFL thinning rates [mean (95% C.I.)] than HC [1.49 (1.09/1.9) vs 0.49 (0.04/0.93) m lost per year, p=0.001]. MCI showed an RNFL yearly decay [0.94 (0.55/1.33) m] intermediate between AD and HC. MCI patients with an AD CSF (Cerebro-Spinal Fluid) signature showed a significantly accelerated RNFL thinning than other MCI patients (1.31 vs 0.44 μm lost per year, p=0.028). RNFL thinning rates were positively associated with cognitive worsening over time and baseline plasma neurofilament concentrations
Conclusion: Our findings might promote neuro-retina as an easily accessible, reproducible and cost-effective marker of neurodegeneration, able to mirror atrophy and cognitive worsening and to monitor the disease course in AD
Disclosure: Nothing to disclose

EPR-139

Converging longitudinal patterns of atrophy in clinical variants of frontotemporal lobar degeneration

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Background and aims: The aim of this study was to assess longitudinal patterns of atrophy shown by magnetic resonance imaging (MRI) in the cortical and subcortical GM of patients affected by different clinical variants of the FTLD spectrum.
Methods: 59 patients, including 26 with behavioral variant of frontotemporal dementia (bvFTD), 10 non-fluent/agrammatic variant of primary progressive aphasia (nfvPPA), 12 semantic variant of PPA (svPPA), and 11 MND, in the absence of known pathogenic mutations, underwent MRI on a 3T scanner at 6-month intervals for one year. Thirty-three healthy controls underwent the same protocol. 3D T1-weighted MRI sequences were analyzed using voxel-based morphometry to assess the longitudinal evolution of GM atrophy in patients, compared with HC.
Results: At baseline, severe diffuse atrophy of frontotemporal cortical regions and basal ganglia was found in bvFTD, nfvPPA and svPPA groups, whereas MND did not show significant GM atrophy. At 6-month follow-up, bvFTD and PPA showed progression of atrophy in the insular (bvFTD, nfvPPA and svPPA) and anterior cingulate cortices (bvFTD and nfvPPA), bilaterally, as well as in the left caudate nucleus and middle temporal cortex (svPPA). At 12-month follow-up, similar patterns of atrophy progression were found, with the additional involvement of the superior frontal cortical gyri in nfvPPA, and right hippocampus in svPPA. No significant progression of atrophy was found in MND.
Conclusion: Atrophy of insular and anterior cingulate cortical regions closely reflects the progression of neurodegeneration across the behavioral and linguistic presentations of FTD, in contrast with a substantial sparing of GM in MND.
Disclosure: European Research Council (StG-2016_714388_NeuroTRACK).

EPR-140

Anticoagulants in Atrial Fibrillation in patients with cognitive decline or Dementia

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Background and aims: The connection between atrial fibrillation (AF) and development of dementia has already been described, however data about cognitive decline in patient with AF and concomitant cognitive impairment are not known. Moreover, there is no agreement in the scientific literature about anticoagulants usage in these patients. The recent EAN guidelines on medical management issues in dementia declare that there is only very low evidence in favor of treatment.

Methods: We analyzed cognitive impairment progression in n=90 outpatients with any grade of cognitive deficit regularly seen from January 2015 to July 2020. 45 patients (50%) were affected by AF (AF + vs. AF-). AF+ and AF- patients were matched 1:1 for sex, age, years of education and MMSE at presentation. Cognitive worsening was inferred using Mini-Mental State Examination (MMSE) score collected in subsequent visits, calculating the Disease progress DPI (MMSE decline over time).

Results: Disease progression index (DPI) in AF+ was three times faster than in AF- patients (-0.1±0.25 vs. -0.06±0.24, AF+ vs. AF-, respectively; p=0.02 2-tailed Student's t-test) (Figure 1). Among the FA+ patients in this study, seven did not take any anticoagulant treatment; the usage of anticoagulant did not show any significant between-group difference in cognitive decline (figure 2).

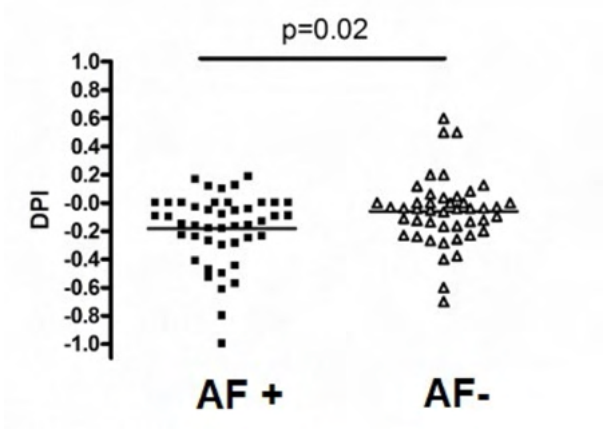

Figure 1. 2-tailed Student's t-test. AF+ = patients with AF. AF- = patients without AF. DPI = disease progression index (MMSE score drop divided by follow-up time)

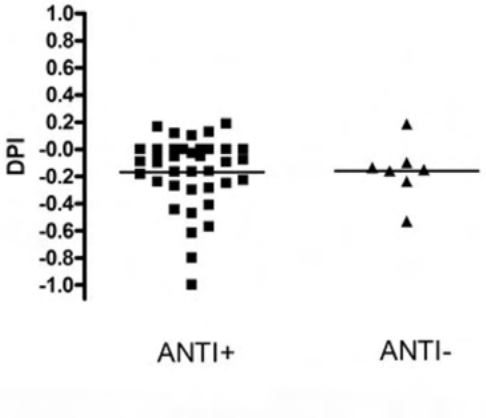

Figure 2. Two-tailed Student's t-test. ANTI+ = patient with AF taking anticoagulants. ANTI- = patient with AF not taking anticoagulants. DPI = disease progression index (MMSE score drop divided by follow-up time)

Conclusion: Our results confirm that AF is a worsening factor in global cognitive function and suggest that the usage of anticoagulants may not significantly affect cognitive decline. We are currently collecting data to increase the sample size and verify our preliminary results. Do not suggest that antico may affect.

Disclosure: No disclosure to decleare

EPR-141

Is language affected by white matter brain damage in Alzheimer`s disease and mild cognitive impairment?

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Background and aims: Impaired language is part of neuropsychilogical presentation of mild cognitive impairment (MCI) and Alzhemer`s disease (AD). Until now, diffusion tensor imaging (DTI) studies didn`t reach consensus about association of impaired language and disrupted white matter brain fibers in MCI and AD.

Methods: 90 people were divided into three groups (AD patients, MCI patients and healty controls) and underwent neuropsychological testing and DTI scan. Cognitive domain Language was composed by using total scores of Boston Naming Test (BNT) and fonemic fluency test. DTI regional diffusion metrics (fractional anisotropy, mean diffusivity, radial and axial diffusivity) were calculated for each of 29 region of interest (ROI). Neuropsycological and DTI metrics were compared between groups by using Kruskal Wallis non-parametric test and correlation between Language domain and DTI metrics in AD and MCI groups was assessed using Spearmans or Pearsons correlation coefficient.

Results: Language domain showed significant difference between all three groups. MCI group showed significantly different DTI metrics in the fornix, while AD group showed differences widely in white matter brain network in majority of DTI metrics. In MCI group, language impairment correlated with left-sided tracts: inferior and superior fronto-occipital and uncinate fasciculus, parahippocampal cingulum and anterior and posterior corona radiata, while AD patients had one significant correlation of language domain and left fornix-stria terminalis.

Conclusion: While language is impaired in all patients, significantly different DTI metrics is present in more ROIs in AD compaired to MCI patients. There is left-sided predominance of white matter brain damage correlating languge impairment in MCI patients.

Disclosure: Nothing to disclose.

Epilepsy 3

EPR-142

Aberrant differential DNA methylation in hippocampus and neocortex of MTLE-HS – a high-throughput single-CpG evaluation

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Background and aims: The etiologic conceptualization of Mesial Temporal Lobe Epilepsy with Hippocampal Sclerosis (MTLE-HS), the most common focal epilepsy, relies on a complex heterogeneous multifactorial model, with epigenetic reprograming gathering special attention.
Methods: DNA methylation profiling was performed with Infinium HumanMethylationEPIC BeachChips in hippocampal and neocortical brain tissue samples of 12 MTLE-HS patients subjected to resective surgery. Control samples from the same regions were obtained from eight autopsied individuals with no neuropathology. Differentially methylated CpG positions (DMPs) were identified by adjusted p (FDR) <0.05 and the difference in average beta values (beta) >0.05.
Results: In the hippocampus, we observed 5,523 DMPs in MTLE-HS vs controls. In the adjacent neocortex, altered DNA methylation was even more significant, with 5,1906 DMPs. We observed an overlap in 1632 hypermethylated and 2,134 hypomethylated CpGs across both tissues. Enrichment was shown for Gene Ontology (GO) terms related to axon morphology, synaptic plasticity, insulin metabolism, cell-cell adhesion, cholecystokinin receptor activity, lipid metabolism, neuroinflammation and neurodegenerative Human Phenotype terms (e.g., EEG abnormality).
Conclusion: A single-CpG resolution methylation evaluation in brain tissue of MTLE-HS patients was amiss. As the pathology's epicenter, the sclerotic hippocampus appears to be modulated by altered DNA methylation patterns encompassing widely described epileptogenesis-related pathways. It is evident that the neocortex, adjacent region more spared from histopathological damage, may partake in neuroexcitibility as they share the said epigenetic traits. The significantly higher differences in DNA methylation in the neocortex lead us to speculate on the relevance of this epigenetic mechanism in the early stages of seizure development.
Disclosure: R.M.-F. is funded by FCT (Fundação para a Ciência e Tecnologia) fellowship (grant number SFRH/BD/137900/2018).

EPR-143

Clinical features and longterm outcome of recurrent Status Epilepticus

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Background and aims: little is known about Status Epilepticus (SE) recurrence. We evaluated the clinical features and the longterm outcome of patients with recurrent SE and assessed the risk of recurrence after an incident event.
Methods: we reviewed our prospective register of consecutive SE episodes of adult patients admitted to the OCB hospital (Modena, Italy), from September 1st 2013 to April 30th 2020. A comparison between recurrent (rSE) and incident SE (iSE) was performed, while the risk of recurrence was evaluated through a survival analysis. Post-anoxic events were excluded.
Results: 535 patients were observed. 43 patients (mean age: 69 y/o, 67% female) experienced SE recurrence, whereas 420 patients (mean age: 71 y/o, 61% female) presented an incident event. Among demographic and clinical variables, an acute symptomatic etiology was less frequently observed in relapsing patients (p<0.01), without differences in terms of previously known epilepsy (p=0.32). The highest risk of recurrence was observed in the first six months following the incident SE (7.7%), whereas the cumulative recurrence rate in our population was 1.5%, 9.2%, 13%, and 15.6% at 30-days, six months, one year, and 3-years respectively. Among rSE, a trend for a late recurrence was associated with a remote symptomatic etiology (p=0.08). Comparing iSE and rSE, we did not find any differences in terms of longterm survival (p=0.69).
Conclusion: SE recurrence was less frequently observed after an acute symptomatic incident event, it was often experienced during the first six months of follow-up and apparently did not influence longterm survival in our cohort of patients.
Disclosure: Nothing to disclose

EPR-144

The National Audit of Seizure Management in Hospitals – Round 3 (NASH 3)

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Background and aims: Seizures are a common presentation in the Emergency Department (ED). Previous rounds of NASH (2011 and 2013) identified major deficiencies in the provision of care and a disconnection between acute medicine and neurology services. Has there been any improvement?
Methods: Setting: 137 Hospital sites across the UK. Participants: 4,132 attendances between 01/06/2018 – 30/06/2019 were assessed, 61% had a prior diagnosis of epilepsy and 23% presented with suspected 1st seizure. Outcome Measures: Data were recorded to assess prior care, the acute presentation and subsequent care including referral for specialist review.
Results: For patients presenting with 1st seizure, neurological examination was documented in 73% and an attempt made to contact an eyewitness in 70.4%. CT Brain was requested in the ED in 66%, which has increased from 55% in NASH 2 and 45% in NASH 1. Onward referral for specialist review was requested in 64%. For patients with epilepsy 55% had not seen an epilepsy specialist in the previous 12 months. CT Brain was requested in 30%, increasing from 22% in NASH 2 and 17% in NASH 1. Specialist review was requested for 35% who had not seen a specialist in the previous 12 months and for 44% who had.
Conclusion: There has been little improvement in the past decade. Improvements are urgently needed to improve the wellbeing of patients presenting with seizures, patients with epilepsy and the efficiency of the healthcare system. Key recommendations include implementing referral pathways, appropriate imaging in the ED, and improved equity of access to services.
Disclosure: Funding to complete the audit was provided by UCB Pharma

EPR-145

The Mozart effect. Why is Mozart better than Haydn?

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Background and aims: Music exposure is a potential method of therapy in neuropsychiatric diseases including epilepsy. We raised the hypothesis that the 'Mozart effect' can be explained by the music's acoustic properties.
Methods: Eighteen epilepsy surgery candidates with intracerebral electrodes implanted in the temporal cortex listened to the Mozart's Sonata for Two Pianos K448 and to the Haydn's 'Surprise' Symphony. Musical features with respect to rhythm, melody, and harmony were analysed.
Results: Epileptiform discharges (ED) in SEEG were reduced by Mozart's music. Listening to Haydn's music led to reduced ED only in the women; in the men, the ED increased. The acoustic analysis revealed that non-dissonant music with a harmonic spectrum and decreasing tempo with significant high-frequency parts has a reducing effect on ED in men. To reduce ED in women, the music should additionally be, in terms of loudness, gradually less dynamic. These acoustic characteristics are more dominant in Mozart's music than in Haydn's music. The fMRI brain activation during listening to music showed stronger functional connectivity in salient, sensorimotor and memory networks in 20 professionals as compared to non-musicians. In men more frontal and in women more parietal areas were activated
Conclusion: We confirmed the 'Mozart effect' in epilepsy. The acoustic characteristics of music are responsible for supressing brain epileptic activity. We suggest the use of musical pieces with well-defined acoustic properties and well-defined characteristics of studied persons are important for studying the 'Mozart effect' in neuropsychiatric diseases.
Disclosure: Nothing to disclose

EPR-146

Item 4 of the NDDI-E for rapid suicidality screening in Russian patients with epilepsy

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Background and aims: Numerous studies have revealed a link between epilepsy and increased risk of suicide. Therefore, it is essential to screen people with epilepsy (PWE) for suicidality with fast screening tool. Item 4 of the Neurological Disorders Depression Inventory for Epilepsy (I4-NDDI-E) "I'd be better off dead" has shown to be an effective screening instrument in European and Chinese populations, but was not tested in the Russian population yet. We aimed to investigate the Russian version of I4-NDDI-E as a suicide screening instrument in PWE.
Methods: A consecutive cohort of PWE admitted to Moscow Clinical and Research Centre for Neuropsychiatry was evaluated with the Suicidality Disorders Module of the Mini International Neuropsychiatric Interview (MINI) and the I4-NDDI-E. A moderate to high suicidality risk, according to MINI, was used as the gold standard. Receiver operating characteristic (ROC) analyses for 4I-NDDI-E scores was used as a statistical method.
Results: The cohort consisted of 214 PWE: 140 (65.4%) male; mean age 40.7 (14.7); 187 (91.2%) with focal epilepsy; mean age at onset of epilepsy 24.8 (16.8). Moderate to high suicidality risk was found in 29 (13.6%) PWE. For I4-NDDI-E ROC-analysis showed an area under the curve of 0.878 (95%CI 0.827–0.919) with sensitivity of 82.7% (95%CI 68.2–94.2), specificity of 88.1% (95%CI 82.6–98.5), positive predictive value of 67.8 (95%CI 57.9–76.3), negative predictive value of 94.4(95%CI 88.4–97.4), and the largest Youden index of 0.787 for a cutoff score of >1.
Conclusion: Item 4 of the NDDI-E is a valuable tool for screening suicidality in the Russian population of PWE.
Disclosure: Nothing to disclose

EPR-147

Valproate use in women with epilepsy of childbearing age in Moscow

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Background and aims: It has been recommended that valproate not to be used to treat women with epilepsy of childbearing age (aged 18–45) – WCA. In this pragmatic study we aimed to assess the proportion of WCA in Moscow, treated by valproate in 2018.
Methods: The study population consisted of 1,268 adults with epilepsy aged 18–93, identified in an epidemiological study of epilepsy in Moscow. Data was collected from "Unified medical information analytical system data". Pearson's chi-square test was used to test for significance.
Results: Antiseizure medication was used by 1,127 of 1,268 adults with epilepsy, including 543 aged 18–45 (269 WCA among them). The proportion of valproate use in all PWE aged 18–45 was significantly higher (206, 33%) than in those aged 46 and older (140, 27%), $p<0.05$. In 18–45 age group the number of women on valproate (90, 29%) was significantly lower compared to men (116, 37%), $p<0.05$, while in those aged 46 and older the proportions were similar (73, 20% women and 67, 24% men, $p>0.05$). 42 of 90 WCA on valproate were in drug remission, 33 had genetic epilepsies. Valproate was used as monotherapy in 64 WCA, and only nine and seven respectively used valproate with carbamazepine or lamotrigine (combinations known to be associated with the highest teratogenicity).
Conclusion: Valproate was used in 29% of WCA in Moscow, most likely because of its superior effectiveness in some genetic epilepsies, but mostly as monotherapy. Possible teratogenic effect of valproate should be taken into account when prescribed to WCA.
Disclosure: Nothing to disclose.

EPR-148

Oedema in epileptic patients with calcified Neurocysticerosis as a risk factor for seizures exacerbation.

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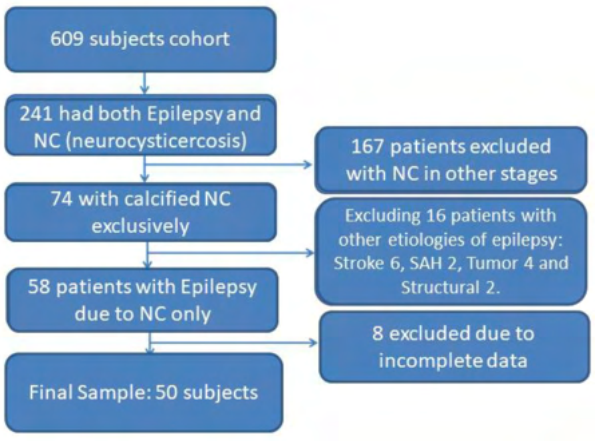
Mexico City, Mexico

Background and aims: Neurocysticercosis (NC) is the most frequent central nervous system parasital disease and epilepsy its most usual manifestation. NC calcifications used to imply absence of inflammation but many researchers have described the presence of oedema surrounding NC calcifications as a potential marker of both inflammation and symptoms augmentation. Until now there is not a clear consensus on how oedema can alter the risk of seizure exacerbation in epileptic patients.

Methods: We performed a case/control study nested inside a cohort using the data obtained from 2,000 to 2,019 by the neurocysticercosis department of the National Institute of Neurology and Neurosurgery in México. "Flowchart-1" shows a detailed explanation of the selection of the subjects. Cases were defined as patients with calcified NC and epilepsy who experimented an augmentation of seizures to two or more per month, status epilepticus or acute repetitive seizures during the follow-up period. Oedema was assessed within the CT or MRI scans of each patient. Baseline characteristics were compared in table 1. The odds ratio for seizure worsening was calculated between cases/controls. Cochran-Mantel-Haenzel test was used to adjust for other confounders such as infection, metabolic disorder, medication reduction, etc.



Flowchart 1. Patients selection for the study

Results: From 50 selected patients, 23 fulfilled case definition. Baseline characteristics didn´t show any relevant imbalance between groups. The risk for seizure exacerbation with oedema was OR:5.35 [CI:1.58–18.06 p<0.01]. When adjusted to other confounders the OR was 5.41 [CI: 1.59–18.38 p<0.007].

Baseline Characteristics	Controls (27)	Cases (23)	p-values
Women (%)	16 (59.3%)	12 (52.2%)	0.77
Median of age (DE)	43.4 (+/- 13.6)	38.5 (+/- 10.6)	0.16
Number of calcificacions (median)	7.33 (2)	8.3 (1)	0.096
CT scan(%)	26 (96.3%)	21 (91.3%)	0.58
MRI(%)	20 (74.1%)	18 (78.3%)	1.0
Calcifications Sites (%)			
• Frontal	17 (63%)	18 (78.3%)	0.35
• Temporal	11 (40.7%)	10 (43.5%)	1.0
• Parietal	14 (51.9%)	15 (65.2%)	0.39
• Ocipital	11 (40.7%)	16 (69.6%)	0.052
• Núcleos de la base	6 (26.2%)	6 (22.1%)	1.0
Edema Sites (%)			
• Frontal	5 (18.5%)	6 (26.1%)	0.73
• Temporal	1 (3.7%)	1 (4.3%)	1.0
• Parietal	0 (0%)	3 (13%)	0.09
• Occipital	1 (3.7%)	4 (17.4%)	0.16
• Base ganglia	0 (0%)	2 (8.7%)	0.20
Seizure onset (%)			
• Focal motor	5 (18.5%)	6 (26.1%)	0.73
• Focal sensitive	2 (7.4%)	3 (13%)	0.65
• Focal visual	0 (0%)	2 (8.7%)	0.20
• Generalized with unknown onset	16 (59.3%)	11 (47.8%)	0.57
• Multiple seizure types	4 (14.8%)	1 (4.3%)	0.35
Treatment (%)	25(92.6%)	21 (91.3%)	1.0
• Monotherapy	14 (51.9%)	15 (65.2%)	0.39
• Dual therapy	8 (29.6%)	7 (30.4%)	1.0
• Triple Therapy	1(3.7%)	0 (0%)	1.0

Table 1. Baseline Characteristics

Edema	Control	Case	Total
Yes	7	15	22
No	20	8	28
Total	27	23	50

Contingency Table 1

Conclusion: We established a 5-fold rise in the independent risk for seizure exacerbation within patients with oedema in calcified NC.

Disclosure: No disclosures are reported for the present study.

Headache and Pain 3

EPR-149

Atogepant Significantly Reduces Mean Monthly Migraine Days in the Phase 3 Trial, ADVANCE

J. Ailani [1], R. Lipton [2], P. Goadsby [3], H. Guo [4], R. Miceli [4], L. Severt [5], M. Finnegan [4], J. Trugman [4]
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Background and aims: Atogepant is an oral, small molecule, CGRP receptor antagonist in development for the preventive treatment of migraine. We evaluated the efficacy, safety, and tolerability of atogepant over 12 weeks.
Methods: Phase 3 trial (NCT03777059). Adults with 4–14 migraine days per month were randomized 1:1:1:1 to once daily atogepant 10mg, 30mg, 60mg, or placebo. The primary endpoint was a change from baseline in mean monthly migraine days (MMDs) across the 12-week treatment period. A key secondary endpoint was the proportion of participants with 50% reduction in their 3-month average of MMDs.
Results: The trial included 910 randomized participants (n=902 safety population, n=873 efficacy analysis population); >87% completed the double-blind treatment period across all groups. Mean change from baseline in MMDs: -3.69 atogepant-10mg, -3.86 atogepant-30mg, -4.20 atogepant-60mg versus -2.48 placebo ($p<0.0001$ all doses). The percentage of participants with 50% reduction in their 3-month average of MMDs: 56% atogepant-10mg, 59% atogepant-30mg, 61% atogepant-60mg versus 29% placebo ($p<0.0001$ all doses). AEs were reported by 52%–54% of atogepant-treated participants and 57% placebo. The most common AEs were constipation (7%–8% across doses vs 0.5% placebo) and nausea (4%–6% across doses vs 2% placebo); none were serious. Serious AEs were reported by 0.9% in both atogepant 10mg and placebo; none were reported for 30mg or 60mg. Discontinuations due to AEs: 2%–4% across atogepant groups and 3% placebo. No hepatic safety issues were identified following daily dosing with atogepant.
Conclusion: Atogepant provided statistically significant and clinically meaningful reductions in migraine days in the ADVANCE trial. Atogepant was safe and well-tolerated.
Disclosure: Study was sponsored by AbbVie

EPR-150

A novel scoring approach to identify responders to erenumab in clinical practice

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Background and aims: Migraine preventives are usually considered successful if they reduce migraine days by at least 50%. In this study, we aimed to develop a multidimensional composite score that combines measures that are clinically relevant to establish migraine patients' response to erenumab.
Methods: The primary outcome of the study was erenumab efficacy, established following standard clinical evaluation. A composite treatment response score was calculated as a linear combination of four response criteria evaluating significant changes in migraine frequency, headache frequency, severity of the migraine attack and migraine-related disability. Logistic regression models were run to assess the association of the composite response score, as well as different response criteria, with the primary efficacy outcome. The Brier Score and receiver-operating characteristic (ROC) analyses were performed to assess model discriminative ability.
Results: 78 migraine patients were enrolled in the study. 38 (53%), 42 (68%) and 24 (73%) patients achieved the primary efficacy outcome after three, six and 12 months of erenumab, respectively. The composite response score achieved the lowest Brier scores at each time point, suggesting a higher predictive accuracy. Compared to the other response criteria, the composite response score had the highest AUC values at month three, month six and month 12.
Conclusion: Here, we proposed a simple and exhaustive multidimensional score that is reliable and stable to follow-up migraine patients' treatment response over time. The use of a simple and comprehensive score may facilitate patients' management in clinical practice and may expand patients' access to effective therapies.
Disclosure: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

EPR-151

SAN711, a selective GABAA 3 receptor positive allosteric modulator as a novel treatment for trigeminal neuralgia

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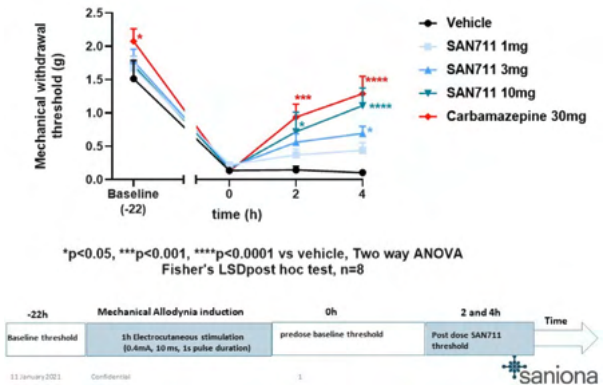
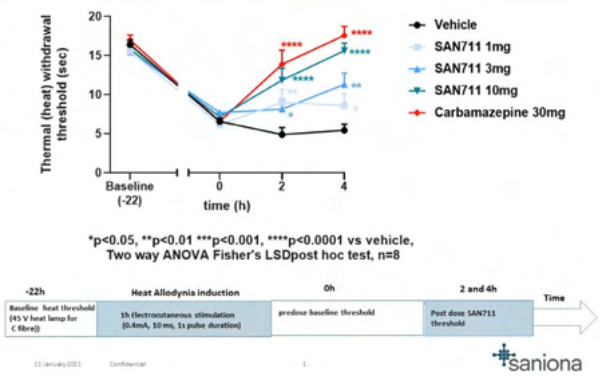
Background and aims: Trigeminal neuralgia is a disorder of the trigeminal sensory system, described as an excruciating, sporadic, and sudden burning facial pain lasting seconds to minutes per episode. Standard of care treatment consists of sodium channel blockers and drugs targeting the GABAergic system. These treatments are non-selective, resulting in dose limiting tolerability issues. We examined the effect of SAN711, a selective GABAA 3 receptor positive allosteric modulator, in a rat model of orofacial pain involving activation of the trigeminal sensory system

Methods: The left depilated cheek of Sprague-Dawley rats was electrocutaneously stimulated and 22 h later facial withdrawal latency was assessed following application of Von Frey filaments for mechanical allodynia and a heat lamp and acetone test for thermal allodynia. SAN711 was administered acutely (1, 3, 10mg/kg, po) after ES and prophylactically (0.3, 1, 3mg/kg, po, QD) for seven days prior to ES. Carbamazepine (30mg/kg, po), the 1st line treatment for trigeminal neuralgia, was used as a reference standard

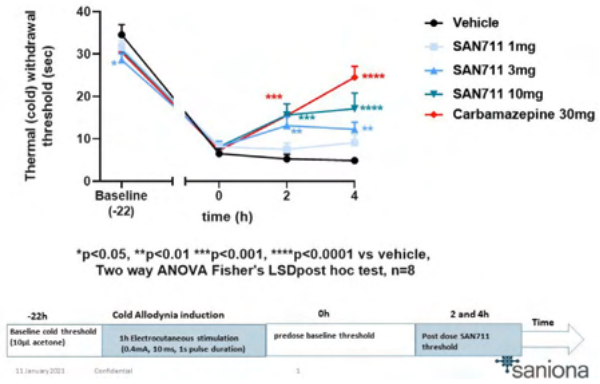
Results: All rats developed ES-induced mechanical and thermal allodynia. Carbamazepine significantly reversed mechanical and thermal allodynia. Acute SAN711 significantly and dose-dependently reversed mechanical and thermal allodynia with a minimum effective dose (MED) between 1–3mg/kg. The highest acute dose of SAN711 (10mg/kg) showed an effect size similar to that of carbamazepine. Prophylactic treatment of SAN711 significantly and dose-dependently prevented development of ES-induced sensitization and lowered the MED to 0.3–1mg/kg.



Dose dependent inhibition of mechanical allodynia by SAN711 in facial pain model of rats



Dose dependent inhibition of heat allodynia by SAN711 in facial pain model of rats



Dose dependent inhibition of cold allodynia by SAN711 in facial pain model of rats

Conclusion: These data support the continued development of SAN711 as a novel treatment for trigeminal neuralgia and other facial neuropathic pain disorders

Disclosure: Nothing to disclose.

EPR-152

Migraine-related healthcare resource use and costs associated with migraine chronification: a panel-based chart review

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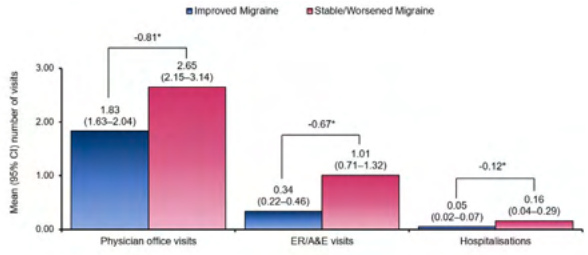
Background and aims: This retrospective, panel-based chart review assessed migraine-related healthcare resource use (HRU) and costs associated with migraine chronification for patients with four or more monthly migraine days (4+ MMDs) in France, Germany, Italy, and Spain.

Methods: Eligible physicians extracted data for adults with 4+ MMDs who initiated one preventive treatment on or after 1/1/2013, and received physician care for six months after the date of the most recent preventive treatment initiation (index date). Migraine-related HRU and costs (2017 €) during the 6-month post-index period were compared between patients with improved versus stable/worsened migraine. Classification was based on the trajectory of migraine severity from the 1-month pre-index period to the post-index period as improved (converting from chronic to episodic or from chronic/episodic to <4 MMDs) or stable/worsened migraine (remaining chronic/episodic or transforming from episodic to chronic).

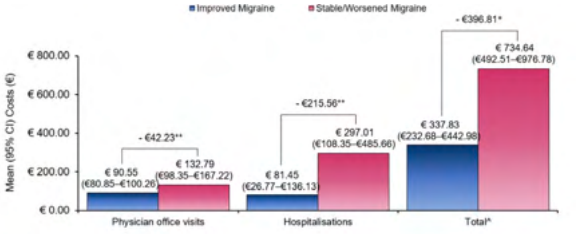
Results: Overall, 470 patient charts (339 improved migraine; 131 stable/worsened migraine) were analysed; mean age was 37 years and 65.7% were female. After adjusting for within-physician correlation, country, sex, and presence of comorbidities, patients with improved migraine had significantly fewer physician office visits (-0.81; p<0.001), emergency room/accident & emergency visits (-0.67; p<0.001), and hospitalisations (-0.12; p<0.001) compared to patients with stable/worsened migraine (Figure 1). Similarly, costs for physician office visits, hospitalisations, and total costs were significantly lower for patients with improved versus stable/worsened migraine (Figure 2).



CI, Confidence interval, ER/A&E, Emergency room/accident & emergency; HRU, healthcare resource use

*p<0.001

Figure 1: Migraine-related healthcare resource use among patients with improved versus stable/worsened migraine (adjusting for country, sex, and presence of comorbidities)



Abbreviations: CI, Confidence interval

**p<0.05, *p<0.01

^Total costs included costs for outpatient visits, emergency room/accident & emergency visits, hospitalisations, nurse practitioner, psychologist, psychiatrist, physiotherapy, or other specialist visits, cranial computerised topography scans, cranial and cranio-cervical magnetic resonance imaging scans, blood tests, nerve stimulator procedures, occipital nerve block procedures, electroencephalograms, and electrocardiograms. However, these costs reflect a conservative estimate. If a physician selected "unknown/not sure" for any healthcare resource item, € 0 was assumed. If healthcare resource unit costs were not available, costs were not included.

Figure 2: Migraine-related costs among patients with improved versus stable/worsened migraine (adjusting for country, sex, and presence of comorbidities)

Conclusion: Over a 6-month period following the initiation of preventive migraine treatment, patients with improved migraine had significantly fewer migraine-related HRU and lower costs than those with stable/worsened migraine.

Disclosure: This study was funded by Novartis Pharma AG, Basel, Switzerland.

EPR-153

6-month efficacy of fremanezumab in migraine patients with inadequate response to ≥3 preventive medication classes

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Background and aims: In 12-week, double-blind period (DBP) of the FOCUS study, fremanezumab, a fully-humanized monoclonal antibody (IgG2a) that selectively targets calcitonin gene-related peptide (CGRP), was effective for migraine preventive treatment in patients with documented inadequate response to 2–4 preventive medication classes. This subgroup analysis evaluated outcomes in patients with inadequate response to ≥3 medication classes during 12-week open-label extension (OLE) of FOCUS.
Methods: Patients were randomized (1:1:1) to quarterly fremanezumab, monthly fremanezumab, or placebo for the DBP. All patients completing DBP entered OLE and received three monthly fremanezumab doses. Changes from baseline (28-day period before first DB dose) during OLE in monthly migraine days (MMDs) and 6-item Headache Impact Test (HIT-6) and Migraine Disability Assessment Test (MIDAS) scores and >=50% response rates (RRs; ≥50% reduction in MMDs) were evaluated in the ≥3 inadequate responses subgroup and summarized descriptively by DB randomization group.
Results: Of 838 randomized patients, 807 completed the DBP and entered the OLE, of whom 405 were included in the ≥3 inadequate responses subgroup. In quarterly fremanezumab, monthly fremanezumab, and placebo DB randomization groups, respectively, LSM(SE) changes from baseline during the 12-week OLE in MMDs were 4.5(0.42), 5.2(0.43) and 4.1(0.48); ≥50% RRs were 39%, 37%, and 28%. LSM(SE) changes from baseline at the end of the OLE in HIT-6 scores were 7.1(0.71), 7.5(0.58), and 5.8(0.67), respectively, and in MIDAS scores were 31.0(4.09), 35.3(4.38), and 24.9(4.48), respectively.
Conclusion: Fremanezumab demonstrated sustained efficacy and improvements in disability over ≤6 months in migraine patients with inadequate response to ≥3 preventive medication classes.
Disclosure: This study and analyses were funded by Teva Pharmaceuticals

EPR-154

Rapid Resolution of Migraine Symptoms After Initiating the Preventive Treatment Eptinezumab During a Migraine Attack

J. Ailani [1], P. McAllister [2], P.K. Winner [3], G.G. Chakhava [4], M.K. Josiassen [5], A. Lindsten [5], A. Ettrup [6], B. Sperling [5], R. Cady [7]
[1] Department of Neurology, Georgetown University Hospital, Washington, DC, United States, [2] Stamford, United States, [3] Palm Beach Headache Center, West Palm Beach, FL, United States, [4] Neurological Service, Tbilisi, Georgia, [5] H. Lundbeck A/S, Copenhagen, Denmark, [6] Valby, Denmark, [7] Lundbeck Seattle BioPharmaceuticals, Inc., Bothell, WA, United States

Background and aims: Eptinezumab is a CGRP inhibitor approved for migraine prevention. An IgG1 monoclonal antibody, eptinezumab is thought not to cross the blood-brain barrier, with the time course of efficacy potentially elucidating peripheral versus central migraine mechanisms. The RELIEF study, which evaluated the efficacy of eptinezumab initiated during a migraine attack, demonstrated that eptinezumab eliminated headache pain and most bothersome symptom (MBS) at 2h postinfusion. The present analysis explored the earliest time points of eptinezumab separation from placebo for headache pain freedom/relief and absence of MBS.
Methods: RELIEF, a multicentre, parallel-group, double-blind, randomised, placebo-controlled trial, assessed the efficacy of eptinezumab 100mg when administered as a preventive treatment during a migraine attack. Treatment was administered over 30-minute IV infusion within 1–6h of migraine onset; study duration was 4–12 weeks. Patients were censored at time of rescue medication use.
Results: More eptinezumab-treated patients achieved headache pain freedom (23/238,9.7%), headache pain relief (92/238,38.7%), and absence of MBS (79/238,33.2%) vs placebo (10/242,4.1%; 65/242,26.9%; 53/240,22.1%, respectively) at 1h ($p<0.05$), with separation continued through 48h. Absence of MBS was achieved earlier by more patients compared with headache pain freedom. For individual migraine-associated symptoms, absence of photophobia and phonophobia with eptinezumab separated from placebo ($p<0.05$) at 1h; separation from placebo for absence of nausea was observed at 0.5h.
Conclusion: Eptinezumab treatment resulted in rapid improvements in headache pain freedom/relief and absence of MBS when administrated as preventive treatment during a migraine attack, demonstrating separation from placebo as early as 0.5–1h following the start of the 30-minute infusion.
Disclosure: H. Lundbeck A/S, Copenhagen, Denmark

EPR-155

The Effect of P2X7 Antagonism on Subcortical Spread of Optogenetically-Triggered Cortical Spreading Depression

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Background and aims: Cortical spreading depression(CSD) is regarded as to be the electrophysiological equivalent of migraine aura. During a migraine attack, symptoms suggesting subcortical dysfunction are observed, some of which are hypothesized to be caused by CSD spread. In this study, the potential role of purinergic P2X7 receptors in the subcortical spread of CSD is investigated using a potent, selective and blood-brain-barrier permeable P2X7 antagonist (JNJ-47965567).

Methods: CSD was optogenetically triggered in adult Thy1-ChR2 transgenic mice. The threshold of CSD was determined by stepwise application of 4mW laser by increasing the duration of laser stimulation (from 0.25 up to 15s). To investigate the subcortical spread of CSD, electrodes were placed in the hypothalamus and cortex and, direct current(DC) shifts were simultaneously recorded. JNJ-47965567 30mg/kg (or its vehicle) was administered 15min prior to CSD intraperitoneally. Cryosections were immunohistochemically labelled for c-fos and imaged with confocal microscope.

Results: The mean optogenetic CSD threshold was 17.92mJ (2.3 SEM, n=14). P2X7 antagonist had no significant effect on CSD threshold and characteristics. In hypothalamus, a DC shift was observed with a mean delay of 51s (4 SEM) relative to the cortical DC shift (CSD). P2X7 antagonism had no significant effect on hypothalamic DC shift as well. Following CSD, c-fos positivity was bilaterally increased significantly in the hypothalamus, suggesting depolarization and neuronal activation, which was prevented by P2X7 antagonist.

Conclusion: P2X7 receptors play a role in neuronal activation in the hypothalamus following CSD; however, it may not have a direct role in the electrophysiological spread of CSD to subcortical structures.

Disclosure: This study was supported by Hacettepe University, Scientific Research Projects Coordination Unit (TSA-2017-14206).

EPR-156

Impact of microvascular decompression on the quality of life of patients with trigeminal neuralgia

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Neurosurgery, St.Petersburg, Russian Federation

Background and aims: Among the pain syndromes caused by damage to the cranial nerves, the main place belongs to the pathology of the trigeminal nerve. According to studies, the average age of development of trigeminal neuralgia is 50.7 years and covers the working, socially-active category of the population. Long-term use of large doses of anticonvulsants reduces the quality of life of patients, often leads to the rejection of daily activities. The most complete result in the treatment is achieved by using microvascular decompression, which ensures a more stable regression of the pain syndrome.

Methods: A clinical study of 32 patients aged 21 to 74 years (median 50.5 years) was conducted. Retrosigmoid access was used in all patients. To assess the effectiveness of surgical treatment, the McGill pain intensity questionnaire and the SF-36 quality of life questionnaire were used.

Results: The patients showed positive dynamics in the late postoperative period in the form of a significant decrease in the sensory, affective and evolutional scales of the McGill pain intensity questionnaire (p0,05). After surgery positive dynamics were revealed on all scales of the SF-36 questionnaire for all 32 patients: an increase in physical, role, social, emotional functioning, a significant decrease in the intensity of pain syndrome (p=0,05).

Conclusion: Microvascular decompression leads to an improvement in the quality of life in the late postoperative period and is an effective treatment method for patients with trigeminal neuralgia.

Disclosure: Nothing to disclose.

Miscellaneous: Critical Care, Neurorehabilitation, Neurotraumatology

EPR-157

Cerebral oedema secondary to hypercapnic respiratory failure in a severe asthmatic attack

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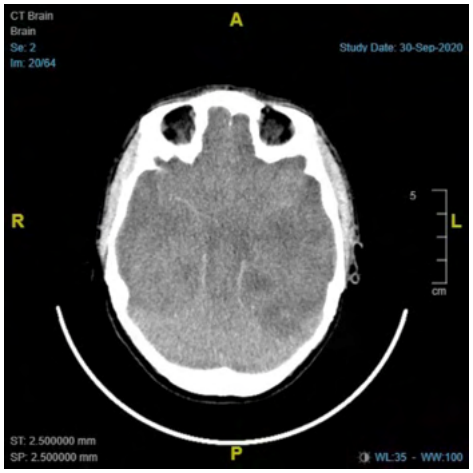
[2] *Department of Medicine, Mater Dei Hospital, Malta, Msida, Malta*

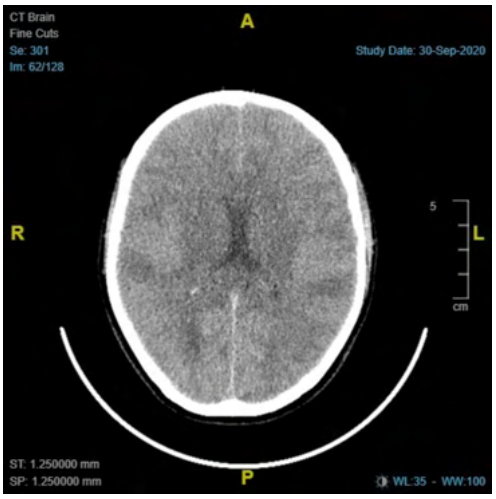
Background and aims: Severe asthmatic exacerbations can be life threatening due the associated type-1 respiratory failure. This can have deleterious effects on the brain. Less frequently, asthma exacerbations may cause hypercapnia. Isolated hypercapnia is seldom documented as the sole cause of cerebral oedema. Our case report highlights the negative effects of hypercapnia in a patient with a severe asthmatic attack.

Methods: A 36 year old asthmatic female, diagnosed in childhood, presented to Emergency department with worsening respiratory symptoms. She had been well controlled on regular reliever medication.

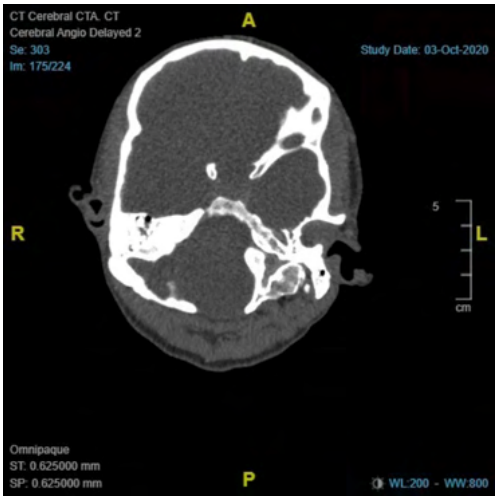
Results: On initial assessment she was found to be in type-2 respiratory failure, with a pH of 7.29 and pCO_2 of 62mmHg. She required immediate intubation and transfer to intensive care. Asthma treatment was maximised. Despite continuous support, type-2 respiratory failure persisted with elevated pCO_2 peaking at 160mmHg. On day 6, she developed polyuria and severe hypernatremia. A CT brain showed extensive cerebral oedema with pseudo-subarachnoid sign. Mannitol was withheld in view of severe hypernatremia. Day 14 into admission, the patient's condition deteriorated; CTA was performed for prognostication which revealed lack of cerebral blood flow.



Non-contrast CT brain showing extensive oedema with pseudo-subarachnoid haemhorrage



Non-contrast CT brain showing extensive brain oedema



CT-angiogram with delayed filling phase showing absence of cerebral vessel perfusion

Conclusion: Isolated hypercapnia as the sole cause of global cerebral edema (GCE) is not commonly reported. Respiratory acidosis and hypercapnia produces vasodilatory effects in cerebral vasculature with resultant brain oedema. Non-traumatic GCE and hypercapnia in the absence of acute brain injury, anoxia, infection, cerebrovascular events is poorly reported. Our case is also unique due to the difficulties encountered to manage cerebral edema by conventional pharmacological agents.

Disclosure: Nothing to disclose

EPR-158

Early predictors of mortality in patients with metabolic encephalopathy

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[1] Neurology Clinic, Belgrade, Serbia, [2] Neurology Clinic, Clinical Center of Serbia, Serbia

Background and aims: : Metabolic encephalopathy (ME) represents a syndrome of temporary or permanent disturbance of brain functions that occurs in different diseases and varies in clinical presentation. It is a severe condition with high in-hospital mortality. The aim of our study was to detect early predictors of in-hospital mortality in patients with ME.
Methods: Our study included 129 consecutive patients with ME treated at our center over a 2-year period. Demographics, clinical, radiological and electrophysiological characteristics on admission and during hospitalization were prospectively collected. Multivariate analysis was used in order to adjust for known confounders and identify predictors of death in patients with ME.
Results: : For the purpose of the study patients were divided in two groups: survivors 96 (74.4%) and deceased 33 (25.6%). In the multivariable logistic regression are included factors that have shown significant in univariate analysis: age, gender, presence of comorbidities, Glasgow coma score and qualitative state of consciousness on admission, presence of paratonia, initial EEG, need for mechanical ventilation on admission. Results of our research demonstrated that older age (OR 1.043, 95%CI 1.003–1.085, p=0.036) and the appearance of 3-phase waves and burst suppression on the initial EEG (OR 4.693, 95%CI 1.479–14.898, p=0.009) stood out as independent predictors of mortality at the beginning of hospitalization.
Conclusion: The study demonstrated that older age and the appearance of three-phase waves and burst suppression on the initial EEG are independent predictors of mortality in patients with ME on admission.
Disclosure: Nothing to disclose.

EPR-159

Anton syndrome in posterior reversible encephalopathy syndrome followed by Guillain-Barré syndrome: a case report.

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Background and aims: Anton-Babinski syndrome is a rare condition due to occipital injury by different mechanisms, such as vasogenic edema in posterior reversible encephalopathy syndrome (PRES) resulting from bood-brain barrier (BBB) disruption. PRES has been rarely associated with Guillain-Barré syndrome (GBS). It has hypothesized that autonomic dysfunction in GBS might lead to BBB damage with consequent PRES before motor symptom onset. Another possibility is that BBB injury in PRES might trigger immune-mediated reaction leading to GBS.
Methods: An 80-year-old woman was admitted to our emergency room (ER) after she developed two partial seizures, successfully treated with 5mg of intravenous midazolam. Her medical history was unremarkable except for previous SARS-CoV-2 disease.
Results: After one hour from midazolam administration, the patient was still markedly confused. Examination revealed binocular blindness, without signs of optic neuropathy; despite being obviously blind, she denied any vision disturbance, a phenomenon known as visual anosognosia. Her blood pressure was 180/90mmHg. Brain MRI showed posterior alterations compatible with PRES. She was treated with antihypertensive and vision recovered after 24 hours. On day 3, she developed areflexia and proximal symmetrical weakness to both upper and lower limbs. Electromyography suggested recent motor poliradiculoneuropathy. Clinical picture was compatible with GBS and intravenous immunoglobulins were started, with gradual recovery. A 8-day follow-up MRI showed nearly complete normalization of posterior lesions.

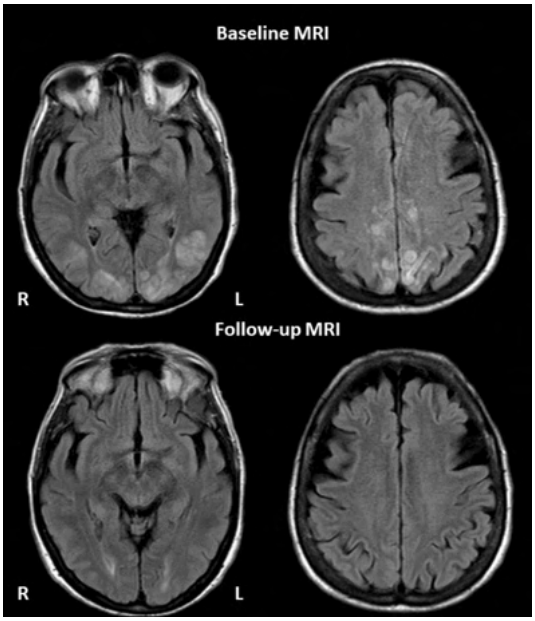

Figure 1

Conclusion: Anton syndrome is a possible rare presentation of PRES. Occurrence of unexplained weakness after PRES should raise suspicion of GBS in consideration of their pathophysiologic connection.
Disclosure: Filippi:Editor-in-Chief JOON;compensation for consulting/speaking activities/research support from Bayer-Biogen Idec-Merck-Serono-Novartis-Roche-Sanofi Genzyme-Takeda-Teva PI;research support from Italian Ministry of Health,FISM,ARiSLA

EPR-160

Outcome of Status Epilepticus admitted to Intensive Care Units (ICU)

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Background and aims: Status Epilepticus (SE) is a neurological emergency with high mortality that often requires admission in Intensive Care Units (ICU). Several factors of worse outcome have been identified in prior studies. A recent study showed a surprisingly higher mortality in the ward than in the ICU but few data are available to explain this mortality after the ICU stay. The aim of our study was to determine the mortality in ICU and in the ward in patients with SE admitted to an ICU and to identify risk factors of mortality.
Methods: Retrospective case series of patients admitted to the ICU for treatment of SE or with SE identified during the ICU stay between January 1, 2015 and December 31, 2019. The primary outcome measure was mortality at ICU or hospital discharge.
Results: Mortality was associated with older age, lower GCS, higher STESS and EMSE scores, NCSE, need for mechanic ventilation and vasopressors, and burden of complications during their ICU stay, but not with refractoriness, or the use of continuous intravenous anesthetic drugs (CIVADs; see Table). No significant difference in clinical features was found between ICU and ward deaths, although ward deaths tended to less frequently have complications during ICU stay than ICU deaths but more frequently compared to survivors.

	TOTAL n = 99	SURVIVORS n = 59	ICU DEATHS n = 31	WARD DEATHS n = 9	p-value (3 groups)	p-value (2 groups)		
						Survivors vs ICU Deaths	Survivors vs Ward Deaths	ICU vs Ward Deaths
Age (years)	63 [49-74.5]	59 [48-66.5]	70 [56-75.5]	70 [59-80]	**0.049**	0.081	0.318	0.795
Pre-admission mRS	1 [0-2]	1 [0-2]	0 [0-3]	0 [0-1]	0.952	0.881	0.795	0.805
Pre-existing Epilepsy	34 (34.3)	24 (40.7)	8 (25.8)	2 (22.2)	0.267	0.161	0.289	0.827
GCS at diagnosis	5 [4.5-10]	8 [6-12]	6 [3-8]	9 [4-9]	**0.022**	**0.013**	0.605	0.387
Refractoriness	65 (66)	38 (64)	19 (61)	8 (89)	0.293	0.771	0.144	0.120
Withdrawal Life Support Therapy	27 (27)	0 (0)	22 (71)	5 (56)	**< 0.001**	**< 0.001**	**< 0.001**	0.385
Scores								
STESS score	3 [2-4]	3 [2-4]	4[3-4]	3[2-4]	**0.004**	**0.010**	0.861	0.152
EMSE score	93 [69-110]	85 [61-98.5]	99 [87-1285]	104 [100-119]	**0.002**	**0.004**	**0.023**	0.746
Charlson Comorbidities Index	5 [3-7]	4 [2-6]	6 [4-7]	5 [4-8]	**0.007**	**0.011**	0.093	0.909
SE types					**0.007**	**0.002**	**0.004**	0.514
GCSE	20 (20)	16 (27.1)	4 (12.9)	0				
Myoclonic	7 (7.1)	0	5 (16.1)	2 (22.2)				
Tonic	1 (1)	0	1 (3.2)	0				
Focal Motor	7 (7.1)	5 (8.5)	1 (3.2)	1 (11.1)				
NCSE in coma	38 (38)	22 (37)	14 (45)	2 (22)				
iGCSE to NCSE	*23 (23)*	*17 (28.8)*	*5 (16.1)*	*1 (11)*				
NCSE non coma	26 (26.3)	16 (27.1)	6 (19.4)	4 (44.4)				
SE etiologies					0.066	**0.039**	0.169	0.605
Acute Symptomatic	61 (61.6)	29 (49.2)	24 (77.4)	8 (88.9)				
Remote Symptomatic	29 (29.3)	24 (40.7)	4 (12.9)	1 (11.1)				
Progressive Symptomatic	1 (1)	1 (1.7)	0	0				
Idiopathic/Cryptogenic	8 (8.1)	5 (8.5)	3 (9.7)	0				
Systemic Treatment								
Mechanic Ventilation	81 (81.8)	43 (72.9)	30 (96.8)	8 (88.9)	**0.017**	**0.006**	0.302	0.339
Vasopressor	57 (57.6)	24 (40.7)	26 (83.9)	7 (77.8)	**< 0.001**	**< 0.001**	**0.037**	0.672
CIVADs	44 (44.4)	24 (40.7)	16 (51.6)	4 (44.4)	0.422	0.195	0.686	0.705
Complications in ICU								
Burden		1 [0-2.5]	2 [1-4]	2 [1-2]	**0.010**	**0.002**	0.991	0.162
- Anemia	36 (36)	14 (24)	17 (55)	5 (56)	**0.006**	**0.005**	**0.048**	0.970
- Any infection	54 (54)	24 (41)	24 (77)	6 (67)	**0.003**	**< 0.001**	0.148	0.512
Complications in the Ward								
Burden	1 [0-2	1 [0-2]		2 [1-3]			0.642	

Comparison of Survivors, ICU and Ward Deaths

Conclusion: Both ward and ICU mortality in patients with SE admitted to an ICU are linked with a more severely etiology and a greater burden of complications during ICU stay rather than the refractoriness of SE itself.
Disclosure: Nothing to disclose.

EPR-161

Interhemispheric substrates of manual dexterity in multiple sclerosis patients: a structural and functional MRI study

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Background and aims: Altered corpus callosum integrity has been associated to impaired hand-motor function in multiple sclerosis (MS). However, a multiparametric advanced-MRI approach has not been applied to investigate its specific contribution to hand clinical impairment. Here, we assessed the transcallosal structural-functional connectivity abnormalities in a large cohort of MS patients and their correlation with different levels of disability and hand-dexterity impairment.
Methods: 3D T1-weighted, diffusion tensor and resting-state (RS) functional MRI scans were acquired from 340 MS patients and 130 age- and sex-matched HC. Probabilistic tractography identified corticospinal tracts (CSTs), transcallosal-fibers between primary hand-motor cortices (M1), supplementary motor areas (SMAs) and premotor cortices (PMCs). Voxel-mirror homotopic connectivity (VMHC) was used on RS fMRI data. Random forest analysis identified independent predictors of different Expanded Disability Status Scale (EDSS) scores (3.0, 4.0, 6.0) and impaired hand-dexterity [9-Hole Peg Test and Finger Tapping (FT)].
Results: Predictors of EDSS-3.0 were global measures of atrophy and lesions together with measures of damage of CST, PMCs and SMAs transcallosal-fibers (out-of-bag (OOB)-accuracy=0.86, p-range=<0.001-0.03). For EDSS-4.0 similar predictors were found, in addition to hand-M1 transcallosal-fibers damage (OOB-accuracy=0.90, p-range=<0.001–0.045). No MRI-variables were identified as predictors of EDSS-6.0. Impaired hand-dexterity was predicted mainly by alterations in SMAs and PMCs transcallosal-fibers (OOB-accuracy-range=0.71–0.76, p-range=<0.001-–0.05), with a specific involvement of hand-M1 transcallosal-fibers in FT-performances. No VMHC-alterations explain the clinical outcomes, even if hand-M1 VMHC resulted abnormal in advanced-disease stages (p=0.045).
Conclusion: In MS patients, only measures of structural damage contribute to explain hand-dexterity impairment and different levels of global disability.
Disclosure: This project has been supported by a research grant from the Fondazione Italiana Sclerosi Multipla (FISM2018/R/5), and financed or co-financed with the '5 per mille' public funding.

EPR-162

Pepperkids – a Next-Gen Social Robot Therapist for Paediatric Neurorehabilitation Processes

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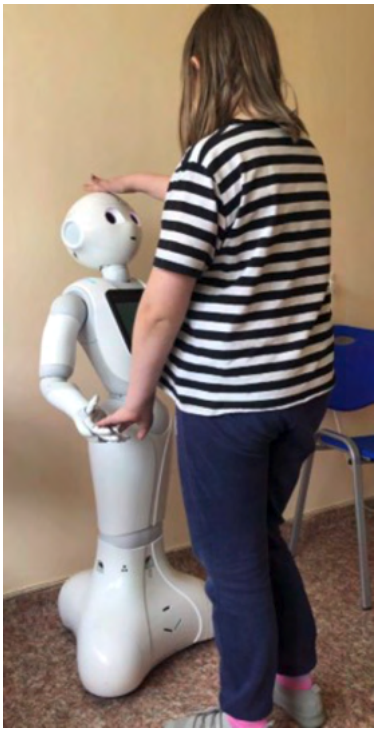
Background and aims: A new challenge in today's paediatric neurorehabilitation is using social robots and evolving AI, which help to teach children verbal and non-verbal communication skills. The main aim of this study was to implement the speaking robot Pepper with the Pepperkids design into the rehabilitation process of children with social communication and speech disorders.

Methods: We used neural speech synthesis technology Neurotolge and collected Estonian children's speech corpus data to create a synthetic child voice, software management framework and programmed behavioral and communication models for Pepperkids. The trainings consisted of ten 30-minute sessions with special topics in communication and language skills, and movement tasks (following Pepper's motions). 10 children aged 5–12 years with different neurological diagnosis have participated in the pilot study.

Results: All 10 children were quickly engaged into the trainings with Pepperkids, without needing extra motivation. Children, who showed defiance prior to the meeting, immediately started to cooperate with the robot. Children expressed similar verbal and non-verbal communication while answering to the robot as for another person: they used full sentences, held eye-contact, laughed etc. Tasks provided on the screen of Pepper's tablet increased emotional and communicational skills. Children gave positive feedback and wanted to return for another session. Still, there is a need for a therapist's presence, who controls the robot and guides the child through the training process.



A patient communicating with social robot Pepper during a Pepperkids session.

Conclusion: The dialogue system between Pepperkids and children is an attractive and more motivating intervention method. Involving social robots would also make the work of the therapists more effective and less time-consuming.

Disclosure: No disclosure.

EPR-163

Cognitive and Neural aftereffects of acute tDCS coupled with cognitive training: An fMRI study in healthy seniors

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Background and aims: Enhancing cognitive functions through non-invasive brain stimulation is of enormous public interest, particularly for the aging population in whom processes such as working memory are known to decline.
Methods: In a randomized double-blind cross-over study we investigated the acute behavioral and neural aftereffects of bi-frontal and fronto-parietal transcranial direct current stimulation (tDCS) combined with visual working memory (VWM) training on 25 highly educated older adults. Resting-state functional connectivity (rs-FC) analysis was performed prior to and after each stimulation session with a focus on the fronto-parietal control network (FPCN). The bi-frontal montage with anode over the left dorsolateral prefrontal cortex enhanced VWM accuracy as compared to the sham stimulation.
Results: With the rs-FC within the FPCN, we observed significant stimulation x time interaction using bi-frontal tDCS. We found no cognitive aftereffects of the fronto-parietal tDCS compared to sham stimulation.
Conclusion: Our study shows that a single bi-frontal tDCS combined with cognitive training may enhance VWM performance and rs-FC within the relevant brain network even in highly educated older adults.
Disclosure: The authors have no conflicts of interest to disclose.

EPR-164

Duration of neurorehabilitation predicts outcome up to ten years after traumatic brain injury

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Background and aims: Traumatic brain injury (TBI) is a major global health burden and patients need multidisciplinary teams to overcome neuropsychiatric sequelae. To date, little is known on how neurocritical parameters influence length of acute treatment and neurorehabilitation. Thus, we investigated this issue and its relevance for functional outcome and health-related quality of life (HRQoL) up to ten years after TBI.
Methods: In this cross-sectional study, neurocritical parameters (TBI severity, intracranial pressure monitoring, tracheostomy, decompressive craniectomy, ventriculo-peritoneal shunt, degree of disability at admission to neurorehabilitation) and patient demographics (age, sex) were investigated in 128 out of 135 TBI patients as predictors for length of acute treatment and neurorehabilitation (multivariate linear regression). Treatment duration was correlated with functional outcome (modified Rankin Scale (mRS)) and HRQoL (QOLIBRI).
Results: Neurorehabilitation started 24.6±1.3 days (mean ± SEM) after TBI and lasted 38.2±2.6 days (mean±SEM). At admission to neurorehabilitation, 96% of TBI patients were severely disabled (mRS 4–5). After neurorehabilitation, 82% of patients were at least able to walk unassisted (mRS 0-3) ($p<0.0001$). Tracheostomy predicts prolonged neurocritical care ($p=0.008$; adj. $R^2=0.08$) and neuro-rehabilitation ($p<0.0001$, adj. $R^2=0.3$). Neurorehabilitation longer than nine weeks correlated with worse functional outcome ($r=-0.4$, $p<0.001$) and unfavorable HRQoL ($p=0.002$) up to 10 years after TBI.

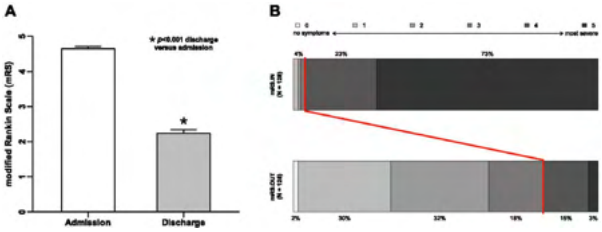

Fig 1. TBI patients recover well from severe disability during neurorehabilitation

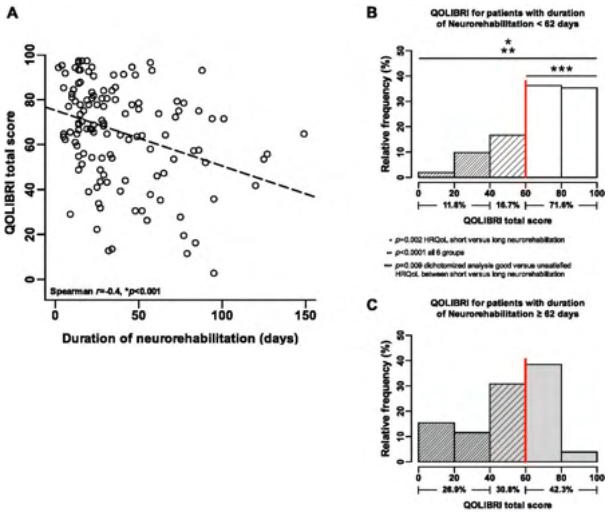

Fig 2. Longer neurorehabilitation correlates with worse health-related quality of life up to 10 years after TBI

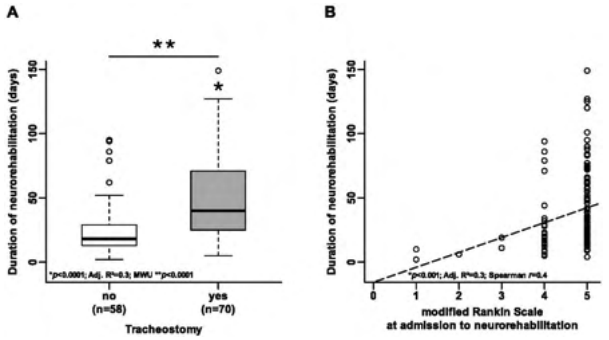

Fig. 3 Tracheostomy and degree of disability predict duration of neurorehabilitation after TBI

Conclusion: Most TBI patients recover well after highly standardized neurorehabilitation, but prolonged neurorehabilitation correlates with unfavorable outcome. Thus, we suggest prolonged neurorehabilitation as a new clinical biomarker to identify patients at risk of unfavorable outcome with the need of neuropsychiatric follow-ups after TBI.

Disclosure: Nothing to disclose

EPR-165

Asymmetric bilateral neuronal loss and neuroinflammation in the hippocampus in acute traumatic brain injury in rats

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Background and aims: Hippocampal disfunction after traumatic brain injury (TBI) may underlie late posttraumatic pathology. However, early dynamics and mechanisms of remote hippocampal damage injury remains obscure. The aim of the study was to assess evolution of morphological damage in neocortex and hippocampus and its biochemical correlates during acute period of TBI in rats.

Methods: The experiment was performed on 48 adults male Wistar rats. TBI was modelled using lateral fluid percussion in the right sensorimotor cortex. The rats were sacrificed on days three and seven after TBI. Blood corticosterone level was measured using ELISA. Brain sections were stained using Nissl method. Microglial activation was assessed by anti-IBA staining. Morphological features of activated microglial cells were assessed.

Results: The density of neurons in the neocortex and ipsilateral dentate gyrus (DG) decreased on day three after TBI and in the contralateral DG on day seven after TBI. Microglial activation was detected only in CA3 area of the ipsilateral hippocampus on day three after TBI, while on day seven it was also evident in the DG of both ipsilateral and contralateral hippocampus. The morphological changes correlated with elevation in blood corticosterone.

Conclusion: Conclusion TBI induce damage in the cortex and remote asymmetric bilateral neuronal loss and neuroinflammation in the hippocampus. The distant TBI-induced hippocampal damage may involve direct and indirect mechanisms.

Disclosure: Supported by RFBR, grant 19-015-00258

Movement disorders 3

EPR-166

Perceived stigma in Parkinson's disease is independent of age and disease duration

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Methods: We asked 62 PD patients to fill out the Stigma in Parkinson's disease scale (STIP), a 23-item questionnaire to gauge self-perceived stigma. The questionnaire was developed based on the Stigma Scale for Mental Health Illness (SSMHI) following a pilot study. Answers were formulated using a Likert scale. Each response was attributed to a numeric value; higher values denote higher perceived stigma. Mean STIP score per patient was determined as a measure of perceived stigma. Correlation between mean STIP and onset age, age, disease duration and Unified Parkinson's disease Rating Scale (MDS-UPDRS) was measured using the Spearman correlation coefficient.
Results: Of 62 patients, 47 (75.8%) were male. Mean STIP score was 2.00±0.61, mean age was 67.2±10.4 years and mean onset age was 57.3±11.9 years. Mean disease duration was 7.6±15.13 years and mean UPDRS score 50.7±22.77. Age (p=0.86), onset age (p=0.61) and disease duration (p=0.92) were not significantly related to STIP. STIP was significantly correlated with total MDS-UPDRS score (rs= 0.34, p=0.009).
Conclusion: In previous studies age, depression and disease duration were reported to predict perceived stigma in PD. With this PD-specific stigma scale, we could not replicate these results. Perceived stigma was moderately related to motor severity. These results suggest that there are more factors influencing stigma perception in PD, requiring future research to focus on a broader scope using PD specific stigma scales.
Disclosure: Funding for this research was granted by the Move for Parkinson patient group.

EPR-167

Role of Parkinson's KinetiGraph in Routine Management of Parkinson's disease

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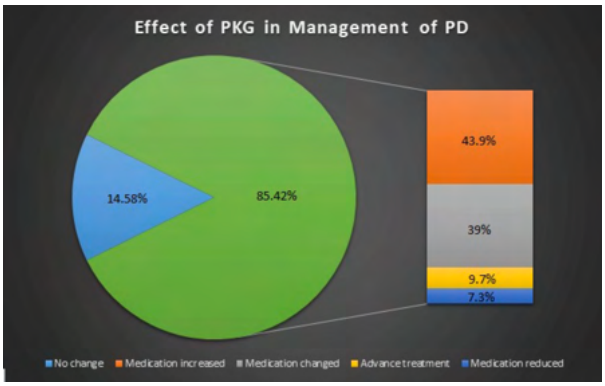
Background and aims: Assessment of Parkinson's disease (PD) in routine clinics lacks objective measurement and largely depends on patient's recall and examination done at that point in time. Variability of motor symptoms demands some form of measurable assessment done over a period. Parkinson's KinetiGraph (PKG) recorded from a wearable device provides this.
Objective: To evaluate the role of Parkinson's KinetiGraph in clinical decision making.
Methods: The outcomes of clinic visits from a single Centre were studied retrospectively for 83 patients who had PKG recorded for seven days. The data was analyzed in terms of any changes made to their management.
Results: 83 patients had PKG and eight patients had more than one recordings. Currently data is available for 48 patients. Out of these 48 patients, changes to medical management were made for 41 patients (85.42%). 18(43.9%) had their medications increased, 16(39%) had medication changed to a different group of medication. 4(9.7%) were referred for advance treatment and 3(7.3%) had their treatment reduced in view of failure to respond and alternate diagnosis was made. No changes were made in the management of seven patients (14.58%)



Effect of PKG in Management of PD

Conclusion: 1. PKG gives a wider picture of motor control of PD symptoms over seven days which helps to improve the medical management 2. PKG can help to identify ICD, drug compliance and compliance to the timing of the medication 3. PKG can be used to reassure the patients. 4. During this pandemic, PKG can be used to monitor patients remotely who are shielding or isolating.
Disclosure: Nothing to disclose.

EPR-168

The Complex Syndrome of Functional Neurological Disorders: Evidence for a Unified Mechanism

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Background and aims: Patients with functional movement disorder (FMD) usually present with multiple motor and non-motor symptoms. This study aimed to determine the presence and nature of correlations between specific symptoms and health related quality of life (HRQoL) and if there were specific clusters of patients based on clinical symptoms.
Methods: 142 patients with clinically established FMD (100 females, mean age 46.4 (SD=12) years; mean disease duration: 6.5 (SD=7.2) years) were assessed for motor phenotype, motor symptom severity using The Simplified FMD Rating Scale, and gait disorder severity. All patients subjectively evaluated motor symptom severity, depression, anxiety, pain, fatigue, cognitive complaints, and HRQoL.
Results: Objectively assessed motor symptoms severity correlated with subjectively reported motor symptoms severity (P<0.001) and with all self-reported non-motor symptoms severity (P<0.001) except for fatigue. All motor symptoms measures showed significant correlation with HRQoL measures (P<0.001), however, only the subjectively reported severity of motor symptoms along with fatigue, pain and depression sufficiently predicted

HRQoL. Hierarchical cluster analysis supplemented with the gap statistic revealed the patient sample was relatively homogenous and could not be separated into subgroups.

Conclusion: Lack of clusters along with high degree of correlation between the self-reported and objective measures of motor or non-motor symptoms and HRQoL could be interpreted within the current neurobiological models suggesting a unied pathophysiology of all "functional" symptoms across the motor, sensory, cognitive and interoceptive domains. Our results support the unification of functional and somatic syndromes which are currently classified separately in current international diagnostic classification schemes.
Disclosure: Supported by Project AZV NU20-04-00332.

EPR-169

Directional and conventional stimulation of subthalamic nucleus in Parkinson's disease (PD): preliminary findings

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Background and aims: New era in subthalamic deep brain stimulation (STN-DBS) appeared to be the introduction of segmented electrodes, which allow steering electric field in a certain direction horizontally. We aimed to assess efficacy and programming features of STN-DBS using segmented(directional) or conventional(omnidirectional) electrodes in advanced PD-patients.
Methods: We included 40 PD-patients who underwent bilateral STN-DBS. In 20 patients, segmented 8-contact electrodes were implanted (age at surgery 54.9±9.5years, disease duration 13.2±4.3years, Hoehn&Yahr 3.2±0.5). In the other 20 patients, conventional 4-contact electrodes were used (age at surgery 57.4±9.0years, disease duration 11.4±4.7years, Hoehn&Yahr 3.2±0.5). Neurological examination was performed preoperatively and after 6-month continuous STN-DBS. We analyzed intraoperative strategy, primary and following settings adjustments, and outcome in each patient.
Results: During initial programming, all electrodes were carefully checked for the best stimulation level, the segmented ones for the best stimulation direction. Directional stimulation was preferentially used if better efficacy or minimization of DBS-induced side effects could be achieved. Directionality was employed in nine patients at 3-month and 6-month follow-up. Following 6-month STN-DBS, patients experienced amelioration of parkinsonian symptoms in OFF-medication state with no significant difference between two groups. Mean OFF-state UPDRS-3 decreased by 66.3% and UPDRS-2 by 59.8% in patients with segmented electrodes compared to 73.9% and 55.7%, respectively, in patients with conventional. Mean LEDD reduced from 1,700 to 735mg and from 1,759 to 581mg, respectively ($p>0.05$).
Conclusion: Efficacy of STN-DBS via segmented electrodes might be comparable to traditional omnipolar stimulation in short-term follow-up. Directional stimulation provides additional possibilities for programming and optimizing STN-DBS outcome.

EPR-170

Defective somatosensory inhibition and plasticity are not required to develop dystonia

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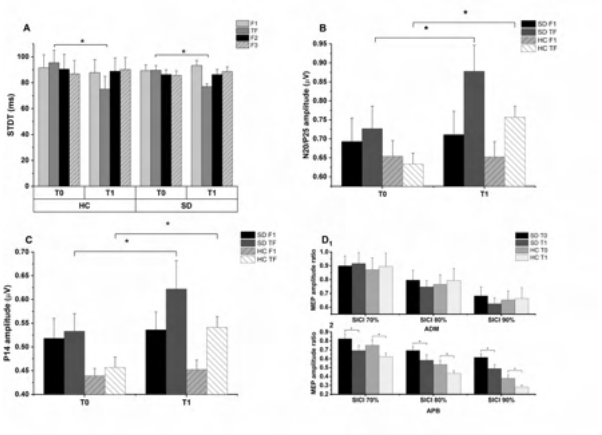
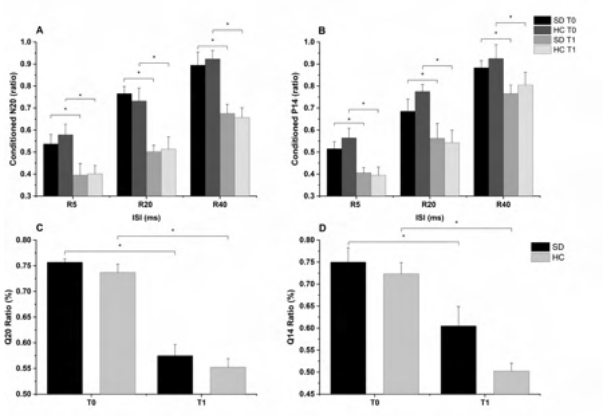
Background and aims: Dystonia may have different neuroanatomical substrates and pathophysiology. This is supported by studies on the motor system showing, for instance, that plasticity is abnormal in idiopathic dystonia, but not in dystonia secondary to basal ganglia lesions. To test whether somatosensory inhibition and plasticity abnormalities reported in patients with idiopathic dystonia, also occur in patients with dystonia caused by basal ganglia damage.
Methods: 10 patients with acquired dystonia due to basal ganglia lesions and 12 healthy controls were recruited. They underwent electrophysiological testing at baseline and after a single 45 minute session of high-frequency repetitive somatosensory stimulation. Electrophysiological testing consisted of somatosensory temporal discrimination, somatosensory evoked potentials (SEP) (including measurement of early and late high-frequency oscillations and the spatial inhibition ratio of N20/25 and P14 components), the recovery cycle of paired-pulse SEPs, and primary motor cortex short-interval intracortical inhibition.
Results: Unlike previous reports of patients with idiopathic dystonia, patients with acquired dystonia did not differ from healthy controls in any of the electrophysiological measures either before or after high-frequency repetitive somatosensory stimulation, except for short interval intracortical inhibition, which was reduced at baseline in patients compared to controls.



Panel A: STDT values, Panel B and C: Amplitude of N20/P25 (B) and P14 (C). Panel D: Effect of HF-RSS on SICI



Recovery cycle of N20/P25 (panel A) and P14 (panel B). Depicted in the lower row is the spatial inhibition ratio of N20/P25, (Q20) (panel C), and P14, (Q14) (panel D)

Conclusion: The data show that reduced somatosensory inhibition and enhanced cortical plasticity are (1) not required for the clinical expression of dystonia and (2) that the abnormalities reported in idiopathic dystonia are not necessarily linked to basal ganglia damage.
Disclosure: Nothing to disclose.

EPR-171

Association of rs3756063 with DNA SNCA-intron1 methylation status in human peripheral blood

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Background and aims: Parkinson's disease (PD) is a common neurodegenerative disease associated with the death of dopaminergic neurons in the brain's substantia nigra due to the accumulation and aggregation of the presynaptic protein alpha-synuclein (SNCA). The expression levels of SNCA gene to be controlled by changes in methylation levels of SNCA. At the same time, DNA SNCA-intron1 methylation levels were also associated with rs3756063 genotype in PD patients. Here we genotyped single-nucleotide polymorphism (SNP) rs3756063 and assessed its association with DNA SNCA-intron1 methylation status in CD45+ blood cells from PD patients and control individuals from North-West region of Russia.
Methods: Screening of SNP rs3756063 was carried out among 1,074 PD patients and 480 controls using PCR restriction analysis. CD45+ cells were isolated from peripheral blood by density gradient centrifugation followed by magnetic separation of CD45+ homogeneous fraction. SNCA-intron1 methylation status was determined among 68 PD patients and 77 control individuals using Next-Generation bisulphite sequencing on MiSeq.
Results: An association of SNP rs3756063 with PD in Russian's North-Western region was not found. No effect of rs3756063 genotype on DNA SNCA-intron1 methylation level in comparing PD patients and controls was revealed ($p>0.05$). An increased level of DNA SNCA-intron1 methylation in carriers of the CC genotype compared to carriers of the G allele (GC+GG) in CD45+ cells of control group was detected (=0.001).
Conclusion: Our data suggest association of SNP rs3756063 with DNA SNCA-intron1 methylation status in control group.
Disclosure: This research has been supported by RFBR grants 16-04-01187 and 18-015-00262.

EPR-172

Opicapone Analysis of Health Economic Costs in Parkinson's UK: findings from the OPTIPARK Study

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Background and aims: Opicapone (OPC) proved effective in treating end-of-dose motor fluctuations in Parkinson's disease (PD) patients in two large multinational trials [1,2]. The OPTIPARK study evaluated OPC 50mg in a heterogeneous population of patients treated in real-world conditions [3].

Methods: OPTIPARK was a prospective, open-label, single-arm, multicentre trial conducted in Germany (3-month) and the UK (6 month). Patients with motor fluctuations received OPC 50mg in addition to current antiparkinsonian treatment. Primary efficacy endpoint was Clinician's Global Impression of Change (CGIC) after three months. Secondary efficacy endpoints included a health economic costs evaluation assessed by Client-Service-Receipt-Inventory (CSRI) questionnaire version adapted to assess the influence of the 6-month OPC treatment on the care costs of UK patients.

Results: At baseline (n=128), total service costs during the previous six months were 284,952.79 UK-£, mainly driven by primary and community care doctor (36.3%) and hospital doctor (18.8%) costs. At six month (n=95), total service costs were 121,280.83 UK-£, mainly driven by hospital doctor (23.4%) and primary and community care doctor (23.2%) costs (Table 1). Average total costs at baseline were 13,060 UK-£, including 2,226 UK-£ for formal service and 11,955 UK-£ for unpaid care costs. Average total costs decreased at 6-month in 3,719 UK-£, including a reduction of 987 UK-£ for formal service and 2,920 UK-£ for unpaid care costs (Table 2).

Table 1. Distribution of Service Costs by Visit – Full Analysis Set

	Baseline N = 128	6-month N = 95
Total service costs by visit (UK-£)	**284952.79**	**121280.83**
Hospital doctor, n (%)	53546.36 (18.8)	28339.96 (23.4)
Day patient, n (%)	9680.7 (3.4)	1683.6 (1.4)
Residential care, n (%)	7289.28 (2.6)	2429.76 (2.0)
Inpatient, n (%)	20801.69 (7.3)	24242 (20.0)
General practitioner, n (%)	19430.4 (6.8)	7456.4 (6.1)
Primary/community care doctor, n (%)	103467.05 (36.3)	28103.75 (23.2)
Other health professional, n (%)	14332.57 (5.0)	8286.72 (6.8)
Social care, n (%)	25354.88 (8.9)	183.2 (0.2)
Investigations/tests, n (%)	4277.76 (1.5)	2787.79 (2.3)
Prostheses/adaptations, n (%)	26772.1 (9.4)	17767.65 (14.7)

n: Costs of corresponding service category;

Table 2. Total Service Costs, Formal Service Costs and Unpaid Care Costs – Full Analysis Set

	Baseline	6-month Change from Baseline
Total Costs		
n	128	93
Mean (SD)	13060.31 (33408.05)	-3718.60 (35473.73)
Median	3875.49	-344.81
Formal Service Costs		
n	*128*	*90*
Mean (SD)	*2226.19 (3191.34)*	*-987.41 (4116.02)*
Median	*1127.04*	*-379.86*
Unpaid Care Costs		
n	*116*	*79*
Mean (SD)	*11954.89 (34304.03)*	*-2920.96 (38036.29)*
Median	*2506.00*	*14.00*

n: Number of subjects with data available; SD: standard deviation; Note: A total of two subjects reported co to care because of MSA and additional six subjects reported MSA as reason for extra (informal) care. Care be of MSA was included in unpaid care costs although subjects with MSA were to be excluded from the trial.

Conclusion: In PD patients with motor fluctuations treated in clinical practice, OPC 50mg had an apparent cost-saving impact.

Disclosure: 1.Ferreira et al., Lancet Neurology 2016;15(2):154-165; 2.Lees et al., JAMA Neurol. 2017;74(2):197-206; 3.Reichmann et al., Transl Neurodegener. 2020;9(1):9

EPR-173

Corticobasal syndrome as first manifestation of Fahr Disease. Videographic record of a case.

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Background and aims: Intracranial basal ganglia calcifications are a common finding in routine neuroimaging, generally age-related and without clinical impact. However, the Fahr Disease (FD), a rare neurodegenerative pathology associated with movement disorders/cognitive impairment, typically presents extensive intracranial calcifications. It can be primary (inherited/sporadic) or secondary (hypoparathyroidism, SLE, etc). Corticobasal syndrome (CBS), an infrequent constellation of clinical features (parkinsonism, apraxia, alien-limb), is thought to be specific of tauopathies, and represents the most usual manifestation of Corticobasal Degeneration.
Methods: We present a patient diagnosed with FD, with clinical debut suggestive of CBS.
Results: A 54-year-old male, with family history of early-onset ataxia (3 relatives), presented an asymmetric rigid-akinetic syndrome, with no response to dopamine and early falls. Afterwards, he developed hyperreflexia, dystonia, alien-limb and cognitive impairment, highlighting executive-attentional dysfunction, amnesic deficit and ideomotor asymmetric apraxia (videographic record), fulfilling current criteria (Armstrong-2013) for probable CBS. He showed severe progressive clinical decline the subsequent two years. Cranial CT-scan showed bilateral calcifications in basal ganglia, cerebellum and occipital cortex (Figure-1,2). DaT-scan showed hypocaptation of right putamen and caudate (Figure-3). Upon suspicion of FD, a comprehensive analytical and genetic study (PDGFB, SLC20A2, etc.) were performed, resulting normal.

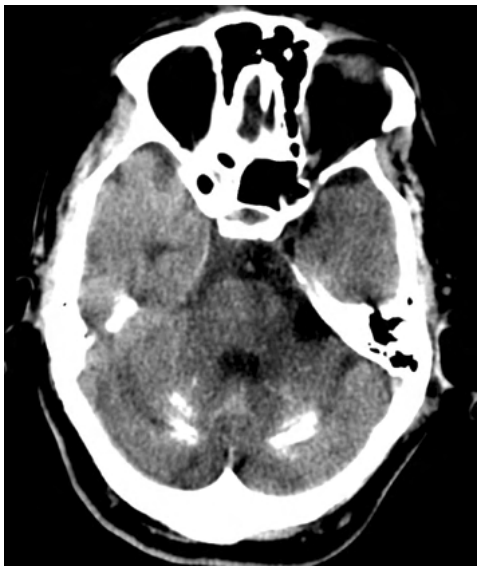

Figure-1

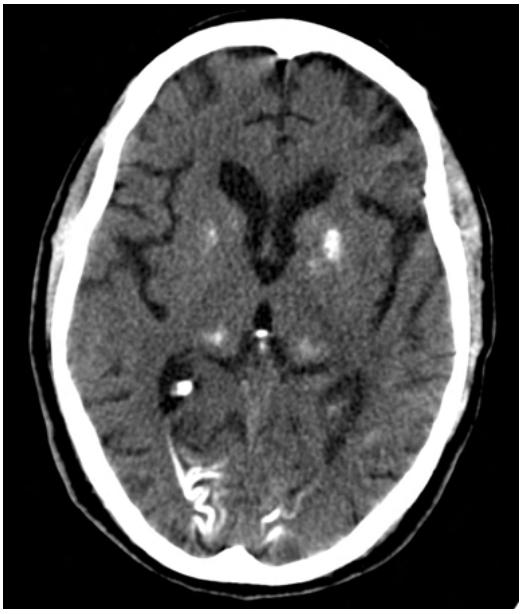

Figure-2

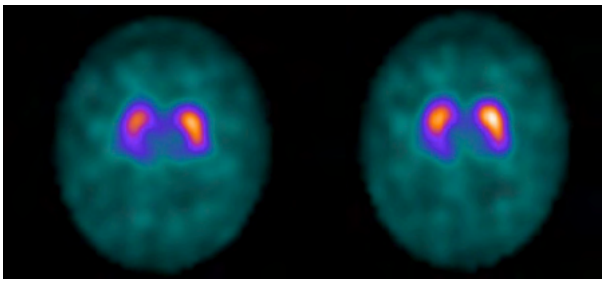

Figure-3

Conclusion: Final diagnostic judgement was probable FD (Manyam-2005 criteria), presenting with CBS. To our knowledge, this association has only been described once before. Our case highlights the hypothesis that CBS, though highly specific, is not exclusive of tauopathies, as FD is not a tau-based pathology. Therefore, in the presence of CBS, an extensive study of secondary (potentially reversible) causes should be carried out.
Disclosure: No disclosures.

EPR-174

Effectiveness of Opicapone in Parkinson's according to baseline use of safinamide: the real-world OPTIPARK study

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Background and aims: Opicapone (OPC) proved to be effective in treating end-of-dose motor fluctuations (MF) in Parkinson's disease (PD) patients [1,2]. The OPTIPARK study evaluated OPC 50mg in a heterogeneous population of patients treated in real-world conditions [3].

Methods: OPTIPARK was a prospective, open-label, single-arm trial conducted in Germany and the UK. Patients with MF received OPC 50mg in addition to current antiparkinsonian treatment. Primary efficacy 3-month endpoint was Clinician's-Global-Impression-of-Change (CGI-C). Secondary efficacy endpoints included Patient's-CGI-C (PGI-C), 8-item PD-Questionnaire (PDQ-8), Unified PD Rating Scale (UPDRS) and Non-Motor Symptoms Scale (NMSS). Safety assessments included evaluation of treatment-emergent adverse events (TEAEs). This post-hoc analysis evaluated, for each outcome, the influence according to baseline use of safinamide (SAF) in patients who completed the study.

Results: 393 (82.4%) patients completed the 3-month endpoint (completers-set, Table 1). Of these, patients NOT using SAF at baseline experienced greater improvements on CGI-C and PGI-C, when compared to patients using SAF at baseline (Table 2). Except for PDQ-8, patients using SAF at baseline experienced greater improvements on UPDRS-II and III, and non-motor symptoms (NMSS), when compared to patients NOT using SAF at baseline (Table 3). Similar incidence of TEAEs considered at least possibly related to OPC were reported for both subgroups (Table 3).

Table 1. Baseline characteristics (Completer-Set)

Category	Used SAF at Baseline N=53	Not Used SAF at Baseline N=340
Age, mean (SD)	66.6 (9.2)	67.2 (9.1)
Male, n (%)	40 (75.5)	217 (63.8)
PD duration, mean (SD) years	8.3 (4.3)	8.4 (4.7)
Onset of MF, mean (SD) years	2.6 (3.2)	2.4 (3.0)
Ldopa amount, mean (SD) mg	572 (223)	556 (251)

SD, standard deviation; PD, Parkinson's Disease; MF, motor fluctuations; SAF, safinamide

Table 2. CGI-C and PGI-C results after 3 months (Completer-Set)

Category	Used SAF at Baseline N=53 n (%)	Not Used SAF at Baseline N=340 n (%)
CGI-C		
Not assessed	-	-
Very much improved	1 (1.9)	29 (8.5)
Much improved	23 (43.4)	144 (42.4)
Minimally improved	19 (35.8)	104 (30.6)
No change	6 (11.3)	50 (14.7)
Minimally worse	3 (5.7)	10 (2.9)
Much worse	1 (1.9)	2 (0.6)
Very much worse	-	1 (0.3)
PGI-C		
Not assessed	-	-
Very much improved	1 (1.9)	29 (8.5)
Much improved	21 (39.6)	138 (40.6)
Minimally improved	20 (37.7)	93 (27.4)
No change	6 (11.3)	52 (15.3)
Minimally worse	3 (5.7)	22 (6.5)
Much worse	2 (3.8)	4 (1.2)
Very much worse	-	2 (0.6)

SAF, safinamide; CGI-C, Clinician's Global Impression of Change; PGI-C, Patient's Global Impression of Change

Table 3. Secondary, after 3 months, and safety outcomes (Completer-Set)

Category	Used SAF at Baseline N=53	Not Used SAF at Baseline N=340
UPDRS II (at ON stage), mean (SD)	-2.0 (4.0)	-1.6 (3.7)
p-value	*0.0007*	*<.0001*
UPDRS III, mean (SD)	-5.0 (10.3)	-4.6 (7.7)
p-value	*0.0009*	*<.0001*
PDQ-8, mean (SD)	-1.7 (11.1)	-3.7 (13.1)
p-value	*0.2858*	*<.0001*
NMSS, mean (SD)	-8.7 (20.0)	-6.5 (20.0)
p-value	*0.0016*	*<.0001*
Any TEAE, n (%)	40 (75.5)	241 (70.9)
At least possibly related[a] TEAEs, n (%)	19 (35.8)	135 (39.7)

SAF, safinamide; SD, standard deviation; UPDRS, Unified Parkinson's Disease Rating Scale; PDQ-8, 8-item Parkinson's Disease Questionnaire; NMSS, Non-Motor Symptoms Scale; p-values obtained through Student's t-test for the change from baseline; [a]relationship to study medication reported as 'possible', 'probable', 'definite' or missing; TEAE, treatment-emergent adverse event (with onset or worsening after first opicapone intake until study termination, either regularly or prematurely)

Conclusion: Overall, these findings indicate that patients may similarly benefit of using or not safinamide and OPC 50 mg as adjunctive therapy to levodopa.

Disclosure: 1.Ferreira et al., Lancet Neurology 2016;15(2):154-165; 2.Lees et al., JAMA Neurol. 2017; 74(2):197-206; 3.Reichmann et al., Transl Neurodegener. 2020;9(1):9

MS and related disorders 3

EPR-175

Improved segmentation of juxtacortical and infratentorial white matter lesions in MS on post-contrast T1 and FLAIR MR

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Background and aims: In patients with multiple sclerosis (MS), the segmentation of juxtacortical and infratentorial white matter (WM) lesions imposes a challenge due to their focal anatomical patterns [1–2]. We evaluated the performance of icobrain ms 5.4 software in segmenting MS lesions on post-contrast T1 MR and FLAIR.
Methods: icobrain ms 5.4 improves its previous versions [3] by incorporating deep learning based on attention-gate 3D U-net to address the challenging segmentation of juxtacortical and infratentorial lesions on post-contrast T1. A dataset consisting of 218 real-world multi-center post-contrast T1 and FLAIR scans from MS patients was stratified in 200 training and 18 validation subjects. We used visually rated lesion segmentations as ground truth, spatially differentiated into four classes: infratentorial, periventricular, juxtacortical, and deep white matter. Furthermore, we used an independent dataset of 67 MS patients with manual segmentation of post-contrast T1 hyperintensities.
Results: The validation dataset results indicated intra-class correlation between automatic segmentation and ground truth of 0.83 and 0.68 compared to 0.3 and 0.5 for the previous version for the juxtacortical and infratentorial WM lesion volumes, respectively. The results in the independent dataset of 67 MS patients showed a median absolute error of 0.18ml and ICC of 0.89 compared to the ground truth for the hyperintensities on post-contrast T1 (figure 1).

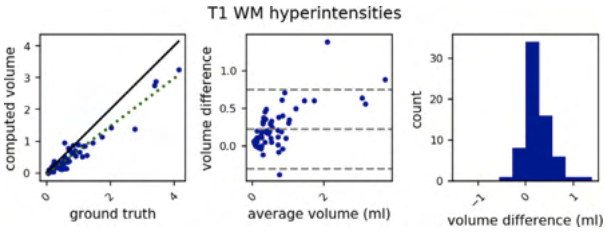

Figure 1: icobrain ms 5.4 performance results for the independent set of 67 MS patients compared to ground truth Left: Scatter plot, Middle: Bland-Altman plots, Right: Histogram of differences between wrt ground truth

Conclusion: icobrain ms 5.4, developed with attention-gate U-net, demonstrated improved MS lesion quantification on post-contrast MR with higher accuracy for juxtacortical and infratentorial WM lesions. References: [1] Coronado et al., (2020). https://doi.org/10.1177/1352458520921360 [2] Hoseinipourasl et al., (2018). https://doi.org/10.31661/jbpe.v0i0.967 [3] Jain et al., (2015). https://doi.org/10.1016/j.nicl.2015.05.003
Disclosure: All the authors are employee of icometrix NV

EPR-176

Association between multiple sclerosis and heart diseases: Systematic review and meta-analysis of observational studies

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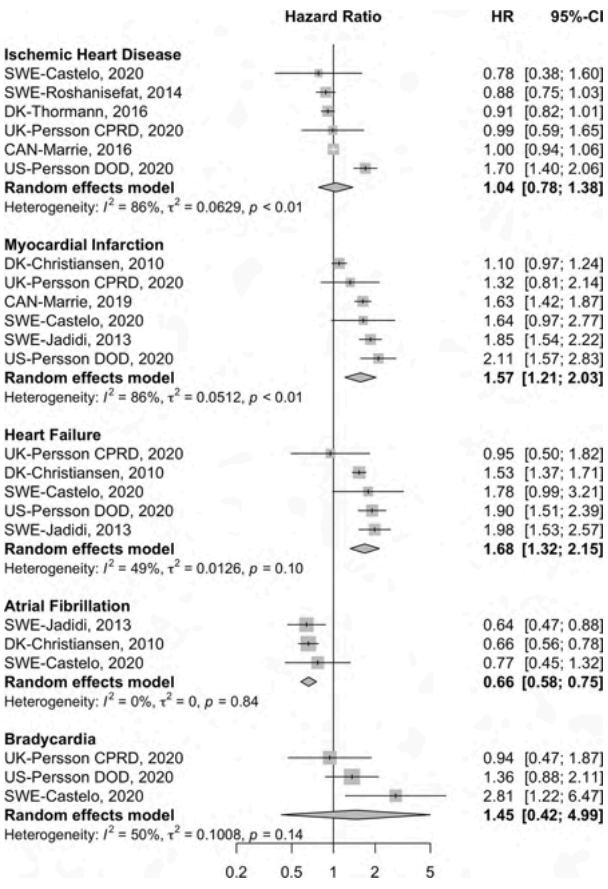
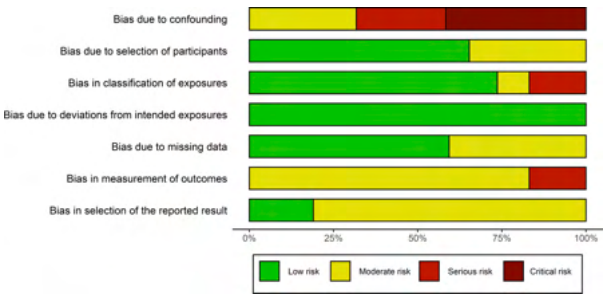
Background and aims: This meta-analysis aims to investigate whether MS is related with heart diseases in observational studies. The outcomes were (i) ischemic heart disease, (ii) heart failure, (iii) myocardial infarction, (iv) cardiac arrhythmia, and (v) infectious heart disease.
Methods: A protocol was published at PROSPERO (CRD42020184493). The systematic literature search included Medline, Embase and Cochrane CENTRAL and was conducted up to 5 October 2020. Non-randomized studies of exposure reporting incident heart diseases were eligible. ROBINS-E was used to assess risk of bias and GRADE to assess the certainty of evidence. Random effect models were used for quantitative synthesis.
Results: Nine studies were eligible for synthesis. The numbers of included individuals ranged between 190 thousand and 1.2 million persons per outcome. We found associations of MS and myocardial infarction (HR 1.6, 95% CI 1.2–2.0, I2 86%), and heart failure (HR 1.7, 95% CI 1.3–2.2, I2 49%) but the certainty of evidence was low. We found no association of MS and ischemic heart disease and bradycardia. The incidence of atrial fibrillation was lower in people with MS but this might be due to critical risk of bias. Infectious heart diseases were only described by one study and were more frequent in people with MS (HR 1.2, 95% CI 1.0–1.4).



Forest Plot



Risk of bias

Conclusion: Higher occurence of myocardial infarctions and heart failure among people with MS should be considered during follow-up examinations. Future studies should consider cardiovascular risk factors as potential confounders.

Disclosure: DR reports no disclosures

EPR-177

Bilateral asynchrony as a marker of upper limb impairments in people with Multiple Sclerosis

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Background and aims: No single objective measure covering the entire range of Upper Limb (UL) functionality in different disability level exists. The aim of the study is to compare synchronised bilateral movements on healthy control (HC) and PwMS using a Inertial Movement Unit (IMU).

Methods: HC and PwMS were assessed through a FNT instrumented version by using a Yost Lab 3-Space™ Sensor Wireless to evaluate bilateral UL coordination. Kinematic parameters were used for the movement analysis (table 1). To evaluate differences depending on disability levels, PwMS were categorized into PwMSLOW (EDSS 5.5) and PwMSHIGH (EDSS 6). The performances of the three groups were compared.

Results: 103 subjects were enrolled: 27 PwMSLOW (EDSS: mean 3.37±1.32, 39F; disease duration: 13.43±11.86 years; 25RR, 1SP, 1PP), 33 PwMSHIGH (EDSS: mean 6.42±0.47; 20F; disease duration: 16.10±8.95 years; 12RR, 14SP, 7PP), 43 HC (mean age: 50.74±16.75 years, 22F). The differences between groups for all parameters of UL function for all the movement phases (going, adjusting, returning) of the FNT for both unilateral and bilateral tasks, right and left arms, for all the parameters are shown in table 2. Significant effect of group, task, arm and the interactions group*task, group*arm, task*arm are summarized in table 3.

Table 1

Outcome Measures	Symbol	Description
Going phase time (ms)	T_{GP}	Time of the hand movement from starting position to nose; time between the first instants in which the angular velocity exceeded and fell below a threshold of 20% of the peak.
Adjusting phase time (ms)	T_{AP}	Time to precisely locate the tip of the nose; time between the end of the going phase and the start of the returning phase.
Returning phase time (ms)	T_{RP}	Time of the hand movement back to the starting position; time between the first instants in which the angular velocity exceeded and fell below a threshold of 20% of the peak.
Total movement time (ms)	T_{TOT}	The movement time of a cycle; it is the sum of T_{GP}, T_{AP} and T_{RP}.
Inter-hand interval (ms) - Going phase	IHI_{GP}	Absolute time difference between the movement beginning of both arms during the going phase.
Inter-hand interval (ms) - Adjusting phase	IHI_{AP}	Absolute time difference between hands for adjusting phase.
Inter-hand interval (ms) - Returning phase	IHI_{RP}	Absolute time difference between the movement beginning of both arms during the returning phase.
Percentage (%) - Going phase	$PERC_{GP}$	Percentage of T_{GP} with respect to T_{TOT}.
Percentage (%) - Adjusting phase	$PERC_{AP}$	Percentage of T_{AP} with respect to T_{TOT}.
Percentage (%) - Returning phase	$PERC_{RP}$	Percentage of T_{RP} with respect to T_{TOT}.

Table 1. Definition of the kinematic parameters calculated on the data from the inertial sensors used in the study.

Table 2

	HC (N=43)	PwMS (N=60)	$PwMS_{LOW}$ (N=27)	$PwMS_{HIGH}$ (N=33)	
Temporal Measures					
Going phase time (T_{GP}) (ms)					
- Unilateral right	527.45 ± 37.25^{b,c}	1042.75 ± 56.88*	981.55 ± 74.90^{a}	1092.82 ± 84.35^{a}	p<0.001
- Unilateral left	473.35 ± 29.74^{b,c}	1057.73 ± 51.11*	1012.49 ± 58.88^{a}	1094.74 ± 80.58^{a}	p<0.001
- Bilateral right	579.62 ± 38.02^{b,c}	1797.35 ± 63.96*	1750.94 ± 61.40^{a}	1835.32 ± 106.37^{a}	p<0.001
- Bilateral left	537.33 ± 25.61^{b,c}	1487.99 ± 45.09*	1462.53 ± 60.93^{a}	1508.82 ± 66.55^{a}	p<0.001
Adjusting phase time (T_{AP}) (ms)					
- Unilateral right	29.46 ± 1.62^{b,c}	148.59 ± 7.68*	139.60 ± 10.22^{a}	155.96 ± 11.30^{a}	p<0.001
- Unilateral left	33.10 ± 1.25^{b,c}	75.11 ± 3.80*	69.05 ± 3.88^{a,c}	80.07 ± 6.12^{a,b}	p<0.001
- Bilateral right	35.28 ± 1.54^{b,c}	291.95 ± 8.06*	288.35 ± 10.30^{a}	294.89 ± 12.26^{a}	p<0.001
- Bilateral left	32.21 ± 1.73^{b,c}	249.65 ± 5.27*	249.64 ± 8.25^{a}	249.66 ± 7.02^{a}	p<0.001
Returning phase time (T_{RP}) (ms)					
- Unilateral right	417.85 ± 27.31^{b,c}	1059.64 ± 64.70*	998.89 ± 91.84^{a}	1109.35 ± 92.11^{a}	p<0.001
- Unilateral left	507.72 ± 27.45^{b,c}	1085.28 ± 49.34*	1052.75 ± 63.71^{a}	1111.89 ± 74.46^{a}	p<0.001
- Bilateral right	458.54 ± 28.60^{b,c}	1758.03 ± 70.46*	1752.55 ± 103.52^{a}	1762.52 ± 99.01^{a}	p<0.001
- Bilateral left	497.38 ± 35.87^{b,c}	1644.16 ± 60.06*	1659.99 ± 94.78^{a}	1631.21 ± 79.51^{a}	p<0.001
Total movement time (T_{TOT}) (ms)					
- Unilateral right	974.76 ± 53.74^{b,c}	2250.99 ± 116.45*	2120.04 ± 159.73^{a}	2358.12 ± 168.62^{a}	p<0.001
- Unilateral left	1014.17 ± 37.39^{b,c}	2218.12 ± 89.77*	2134.29 ± 118.33^{a}	2286.70 ± 133.48^{a}	p<0.001
- Bilateral right	1073.44 ± 47.26^{b,c}	3847.33 ± 105.57*	3791.84 ± 134.43^{a}	3892.74 ± 160.65^{a}	p<0.001
- Bilateral left	1066.91 ± 53.93^{b,c}	3381.80 ± 87.31*	3372.16 ± 138.27^{a}	3389.69 ± 115.29^{a}	p<0.001
Inter-hand interval (ms)					
- Going phase (IHI_{GP})	215.96 ± 28.16*	536.16 ± 56.13*	367.81 ± 53.88^{a}	673.89 ± 86.22^{a,b}	p<0.001
- Adjusting phase (IHI_{AP})	9.73 ± 1.27^{b,c}	68.61 ± 6.93*	59.06 ± 7.29^{a}	76.42 ± 11.12^{a}	p<0.001
- Returning phase (IHI_{RP})	219.78 ± 29.51^{b,c}	550.63 ± 59.85*	527.24 ± 79.19^{a}	569.76 ± 89.50^{a}	p<0.001
Percentage					
Going phase ($PERC_{GP}$) (%)					
- Unilateral right	53.26 ± 1.99^{b,c}	46.83 ± 1.08*	46.74 ± 1.50^{a}	46.91 ± 1.58^{a}	p<0.05
- Unilateral left	46.47 ± 1.98	47.66 ± 1.02	47.40 ± 1.06	47.87 ± 1.68	p=0.844
- Bilateral right	53.81 ± 2.09^{b,c}	46.87 ± 1.22*	46.81 ± 1.53^{a}	46.96 ± 1.88^{a}	p<0.01
- Bilateral left	51.58 ± 1.53^{c}	44.30 ± 0.98*	43.76 ± 1.18	44.75 ± 1.53^{a}	p<0.05
Adjusting phase ($PERC_{AP}$) (%)					
- Unilateral right	3.03 ± 0.03^{b,c}	6.61 ± 0.02*	6.60 ± 0.04^{a}	6.61 ± 0.03^{a}	p<0.001
- Unilateral left	3.27 ± 0.03	3.30 ± 0.05	3.23 ± 0.03	3.36 ± 0.09	p=0.103
- Bilateral right	3.29 ± 0.02^{b,c}	7.59 ± 0.02*	7.61 ± 0.04^{a}	7.57 ± 0.03^{a}	p<0.001
- Bilateral left	3.00 ± 0.03^{b,c}	7.44 ± 0.05*	7.47 ± 0.08^{a}	7.42 ± 0.06^{a}	p<0.001
Returning phase ($PERC_{RP}$) (%)					
- Unilateral right	43.71 ± 1.98	46.56 ± 1.08	46.65 ± 1.50	46.48 ± 1.58	p=0.384
- Unilateral left	50.27 ± 1.98	49.04 ± 1.02	49.36 ± 1.05	48.77 ± 1.67	p=0.825
- Bilateral right	42.90 ± 2.09	45.51 ± 1.23	45.58 ± 1.52	45.46 ± 1.89	p=0.451
- Bilateral left	45.42 ± 1.53	48.25 ± 0.99	48.77 ± 1.20	47.83 ± 1.54	p=0.275

* indicates statistically significant difference between PwMS and HC. a, b, c indicate statistically significant differences at the post hoc analysis with respect to HC, $PwMS_{LOW}$ and $PwMS_{HIGH}$ respectively.

Differences in kinematic parameters between HC and PwMS and among HC and the two PwMS groups after splitting by disability level. The data are shown for each type of task and arm.

Table 3

parameters	group	task	arm	group*task	group*arm	arm *task	group*arm*task
T_{TOT}	X***	X**		X***			
T_{GP}	X***	X*		X***			X*
T_{AP}	X***	X***	X*	X***	X***		
T_{RP}	X***	X**		X***			
$PERC_{GP}$					X**		
$PERC_{AP}$	X***	X***	X***	X***	X***	X***	X***
$PERC_{RP}$							

*p<0.05; ** p<0.01; *** p<0.001

Summary of the three-way ANOVA results for PwMSLOW, PWMSHIGH and HC showing effect of group, task, arm and the interactions group*task, group*arm, task*arm.

Conclusion: Results highlight that the use of an Inertial Movement Unit (IMU) to assess UL function could be a useful methods to discriminate HC from PwMS with different disability level.

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EPR-178

Correlation between subjective and objective measures for upper limb function in multiple sclerosis

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Background and aims: Multiple Sclerosis (MS) is chronic autoimmune disease. Upper limb (UL) function is often affected in people with MS (PwMS); UL is usually assessed with objective measures: Nine Hole Peg Test (9-HPT), Box and Block Test (BBT), Hand Grip Strenght (HGS). Subjective perspective of PwMs must be taken into account. Manual Ability Measure-36 (MAM-36) is self-perceived questionnaire (ability to perform manual activity). The study aims to evaluate correlations between objective (9-HPT, BBT, HGS) and subjective (MAM-36) UL measures to understand impact of UL dysfunction in MS.

Methods: The multicenter study included five Italian neurological centers. Inclusion criteria: age>18, MS diagnosis, stable disease course, signed informed consent. Exclusion criteria: bilateral UL plegia, orthopaedic or neurological diseases not MS. 9-HPT, BBT, HGS, MAM-36 were collected.

Results: 193 PwMS were included: 127 females (n=65.8%), mean age 50.51 years (SD=13.27), 116 relapsing/remitting patients, 29 primary and 48 secondary progressive MS, mean disease duration 14.20 (SD=14.42) years, mean EDSS 4.54 (SD=1.98). Table 1 reports descriptive statistics for UL measures. 9-HPT, HGS, BBT, MAM-36 did not comply with normality. Table 2 shows Spearman correlations in the whole sample, by EDSS and disease course. 9-HPT had significant negative correlations with the MAM-36; BBT and HGS had positive association with MAM-36, except for asymmetry.

Measure	Mean	Standard Deviation	Median	Minimum	Maximum
MAM-36_Rasch score	3.101	2.168	2.64	-2.040	6.650
9HPT					
Dominant	30.44	16.43	25.00	15.00	130.66
Non-Dominant	32.19	18.66	26.00	3.00	146.00
Mean	31.32	14.53	25.50	11.50	92.00
Asymmetry	9.44	17.46	3.00	0.00	108.00
HGS					
Dominant	19.33	9.96	18.00	1.28	52.00
Non-Dominant	17.85	8.70	17.06	1.78	49.33
Mean	18.59	8.78	17.50	2.96	50.67
Asymmetry	4.90	4.44	3.55	0.00	26.93
BBT					
Dominant	47.09	16.78	45.00	12.00	102.00
Non-Dominant	46.54	16.04	46.00	13.00	103.00
Mean	46.82	15.80	45.50	13.00	101.00
Asymmetry	6.26	6.36	4.00	0.00	49.00

Table 1. Descriptive statistics for upper limb measures

	All Patients (N = 193)	Disability: EDSS ≤ 3 (N =60)	Disability: 3.5 - 5.5 (N =50)	Disability: ≥ 6 (N =83)	Disease Course: RR (N = 116)	Disease Course: PP/SP (N = 77)
9HPT						
Dominant Arm	**-.275**	.135	**-.294**	**-.266**	-.182	**-.377**
Non-Dominant Arm	**-.242**	.058	-.070	-.084	-.117	**-.447**
Mean	**-.314**	.090	-.199	**-.282**	**-.204**	**-.483**
Asymmetry	**-.312**	-.083	-.199	**-.341**	**-.278**	**-.353**
HGS						
Dominant Arm	**.326**	**.424**	**.541**	.198	**.477**	.143
Non-Dominant Arm	**.237**	**.332**	**.383**	.066	**.259**	.204
Mean	**.306**	**.382**	**.500**	.173	**.395**	.198
Asymmetry	**-.221**	.050	.056	**-.440**	-.119	**-.334**
BBT						
Dominant Arm	**.347**	.095	.176	**.366**	**.352**	**.272**
Non-Dominant Arm	**.267**	.075	.072	.084	**.252**	**.2335**
Mean	**.328**	.074	.124	**.254**	**.321**	**.275**
Asymmetry	**-.209**	-.023	-.208	**-.292**	-.114	**-.316**

Note. Correlations in bold are significant at p<.05. RR = Relapsing Remitting; PP/SP = Primary and Secondary Progressive.

Table 2. Spearman correlationns between MAM-36, 9-HPT, HGS and BBT in the whole sample, by EDSS level and disease course.

Conclusion: Correlations between objective measures and MAM-36 were small or moderate, meaning that subjective perception is not covered by objective measures.

Disclosure: The study was fund by Intalian Multiple Sclerosis Foundation (FISM)

EPR-179

Efficacy/safety profile of cladribine in an italian real-life cohort of relapsing remitting multiple sclerosis patients

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Background and aims: Multiple sclerosis (MS) is a chronic inflammatory and degenerative disease of the central nervous system. Cladribine (CLD) is an immunosuppressant drug approved for the treatment of MS. We present efficacy/safety profile of CLD in an Italian cohort of MS patients, identifying early predictors of response.

Methods: Demographic, clinical and neuroradiological data were collected from clinical records at San Raffaele Hospital.

Results: Table 1 shows demographic, clinical and neuroradiological baseline characteristics of our cohort (60 patients). 71,2% and 88,2% reached No Evidence of Disease Activity (NEDA-3) at 12 and 24 months. NEDA-3 was more frequently achieved by naïve than switchers (HR 2,1; 95% CI: 1,09-4,04; p=0,03). Mean Annualized Relapse Rate and median Expanded Disability Status Scale (EDSS) according to patients' characteristics during follow-up are summarized in Figure1. No patients presented EDSS progression at 24 months. Neuroradiological findings are summarized in Figure2. 30% showed at least one side effect, e.g. fever/infections, headache, increased liver enzymes, herpes labialis and fatigue. None of them was serious. At month 3, 39,3% presented lymphopenia (mainly grade 1–2, only one patient grade 3). At month 15, 41,6% had lymphopenia (60% grade 2 and only 15% grade 3). No grade 4-lymphopenia cases were observed and no retreatment was delayed due to lymphopenia. None of infections occurred in patients with grade 3-lymphopenia.

Conclusion: CLD efficacy/safety profile in our cohort is similar to previously published data. CLD is more efficacious when used early and is overall well tolerated. Further data and longer follow up are needed to confirm our observations.

N=60	(F= 43; 71,7%)
Age (y), mean ± SD (min-max)	34,7 ± 7,9 (20,3-50,6)
MS Duration (y), mean ± SD (min-max)	7,27 ± 5.54 (1,35-22,92)
EDSS, median (min-max)	2,0 (1,0-6,0)
ARR (mean) in the past 1 year	1,0 ± 0,9
ARR (mean) in the past 2 years	1,8 ± 1,0
Time from MS onset to CLD start (y), mean ± SD (min-max)	5,6 ± 5,5 (0,2-22,7)
Treatment characteristics	**Naive,** number (%) = 29 (48,3%) **Previous treatments**, mean (min-max) = 1,3 (1-4) **Early switch,** number (%)= 10 (16,7%) **Switch from 1° line DMDs** (%)= 16, (26,7%) **Switch from 2° line DMDs,** number (%) = 15, (25,0%) **Previous immunosuppression,** (%) = 3 (5,0%)
Number of T2-weighted lesion, mean (min-max)	32,6 (4,0 -85,0)
Number of Gd-enhancing, mean (min-max)	4,3 (0,0-35,0)
Retreatment (2° year), number (%)	52 (86,7%)
Follow-up (m), mean ± stand dev (min-max)	19,6 ± 7,2 (2,8-32,4)

Table 1. Demographic, clinical and neuro-radiological characteristics of population at baseline.

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EPR-180

Metabolomics of Cerebrospinal Fluid in Patients with Multiple Sclerosis Compared to Healthy Controls: Pilot Study

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Background and aims: Multiple sclerosis (MS) is a chronic autoimmune disease of the central nervous system (CNS) leading to loss of myelin and axons. Diagnosis is based on clinical findings, magnetic resonance imaging and analysis of cerebrospinal fluid (CSF). CSF is ultra-filtrate of plasma and reflects inflammatory processes in the CNS. The aim of this study was to perform metabolomics analysis of CSF in MS patients and healthy controls and try to find new specific analytes for MS.

Methods: We collected CSF of 14 patients (10 females, aged 19–55 years) with newly diagnosed MS and CSF of 12 healthy controls (9 females, aged 29-50 years). CSF samples were analysed using HPLC-MS/MS method in ESI+ and – mode. Data were processed with AB Sciex software. Further, the results were processed with Metaboanalyst database and verified by targeted analysis with analytical standards. In the most of verified results, their levels were compared between the both groups.

Results: We selected 130 analytes, based on some attributes such as p-value, grouping, etc., where we found significant differences between the groups. We found specific analytes increased in MS – stearic, palmitic, and myristic acid, as well as analytes decreased in MS – phenylalanine and tyrosine.

Conclusion: We observed significant differences in CSF of MS patients and healthy controls, mostly in amino acids and fatty acids. Moreover, we found new specific analytes which were increased in MS – stearic, palmitic, and myristic acid. Further analysis are necessary and may help to find a new potential biomarkers specific for MS.

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EPR-181

Rituximab vs. mitoxantrone: comparing efficacy and safety in (advanced) relapsing- multiple sclerosis

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Background and aims: Background: Rituximab (RTX), a CD20 depleting agent, is a frequently used off-label treatment for multiple sclerosis (MS), while mitoxantrone (MTX) is approved, albeit rarely used for active relapsing MS (RMS). However, observational data comparing RTX and MTX efficacy and safety are scarce.

Methods: To compare efficacy and safety of MTX and RTX in patients with active RMS. From combined retrospective clinical data of three MS centers, we selected patients who had received at least one infusion of RTX or MTX and had at least a 6-month clinical follow-up available. Treatment groups were compared by propensity score (PS)-adjusted regression and inverse PS-weighted generalized estimated equation models regarding disability progression, relapse activity, and adverse events (AE).

Results: We included 292 RMS patients (mean age 41.8years, 71.6% female) who received RTX (119 patients, mean age 36.8 years, 74.8% female) or MTX (173 patients mean age 45.3 years, 69.4% female). Using both PS methods, we did not find a significant effect favoring RTX or MTX treatment regarding the probability of disability worsening or relapse occurrence. However, RTX treatment was associated with a significantly lower probability of severe AEs and AEs.

Conclusion: RTX shows comparable efficacy but a favorable safety profile compared to MTX in active RMS.

Disclosure: has participated in meetings sponsored by or received travel funding from Biogen, Merck, Novartis, Roche, Sanofi-Genzyme and Teva.

EPR-182

Evaluating the Effect of BTK Inhibitor Tolebrutinib in Modulating Microglia-Driven Neuroinflammation and MS Progression

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Background and aims: Bruton's tyrosine kinase (BTK) inhibition may provide additional therapeutic benefit to B cell depletion for patients with multiple sclerosis (MS) by modulating microglia-driven neuroinflammation within the central nervous system (CNS). We evaluated the effects of the CNS-penetrant BTK inhibitor tolebrutinib on microglia for its potential to modulate MS disease progression.

Methods: BTK and phospho-BTK were measured using immunohistochemistry, Western blot analysis, and RNA sequencing in microglial cells, mouse brains, and postmortem specimens obtained from patients with MS. Tolebrutinib exposures in cerebrospinal fluid (CSF) samples obtained from humans and nonhuman primates were assessed.

Results: We generated a microglial gene expression signature of BTK signalling using transcriptome analysis. Immunohistochemistry and single-nucleus RNA sequencing (snRNAseq) demonstrated that BTK protein and mRNA were abundant in microglia from autopsy-derived MS lesions relative to control specimens. snRNAseq in brain autopsy samples from patients with progressive MS or control specimens showed that microglial gene expression shifted from a homeostatic phenotype to a reactive and/or inflammatory signature. In vivo, the role of BTK inhibition in modulating neuroinflammation was assessed in mouse brains using a CNS-penetrant BTK inhibitor tool compound. In vitro, tolebrutinib demonstrated subnanomolar BTK binding affinity in human B cell and microglial cell lines with similar potency in biochemical and cellular assays. Phase 1 data demonstrated human CSF concentration of tolebrutinib exposure was approximately 4 nM. Nonhuman primate CSF exposure analysis also showed significant CNS penetration of tolebrutinib.

Conclusion: Tolebrutinib, a CNS-penetrant BTK inhibitor, can modulate BTK-dependent inflammatory signalling in microglia in vitro and in vivo.

Disclosure: STUDY SUPPORT: Sanofi.

Muscle and neuromuscular junction disease 2

EPR-183

Incidence and clinical spectrum of rhabdomyolysis in neurology: a retrospective cohort study

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Background and aims: To evaluate demographic, clinical and laboratory characteristics of patients with rhabdomyolysis in a tertiary neurological center.
Methods: This retrospective cohort study included all patients with serum creatine kinase (sCK) activities >950 U/L treated at the Department of Neurology, Medical University of Vienna, between 01/2000–12/2017. Demographic, clinical and laboratory parameters were extracted from medical records. The incidence of rhabdomyolysis in specific neurological diseases was estimated as the ratio between rhabdomyolysis cases and the total number of cases with the corresponding disease. The time course of sCK activity was plotted for individual patients with serial measurements, and sCK half-life together with sCK steady-state activity seven days after the peak measurement were calculated.
Results: A total of 248 patients with rhabdomyolysis were identified with a median sCK activity of 2,160 U/l (IQR 1,342–4,786). Seizures (31.9%), illicit drugs/alcohol (9.7%) and exercise (8.5%) were the most common trigger factors. Rhabdomyolysis incidence rates were highest in myopathies (49.8/1,000 person-years, 95% CI 32.3–67.4), followed by epilepsy (16.4/1,000 person-years, 95% CI 12.8–20.0) and stroke (11.9/1,000 person-years, 95% CI 8.4–15.4). The half-life of sCK activity was 1.5 days in the total cohort. In myopathies, sCK activity was significantly higher as compared to other disease entities seven days after the peak measurement (p=0.0023). Acute kidney injury (AKI) developed in 18 patients (7.3%) with no AKI-related deaths during the study period.

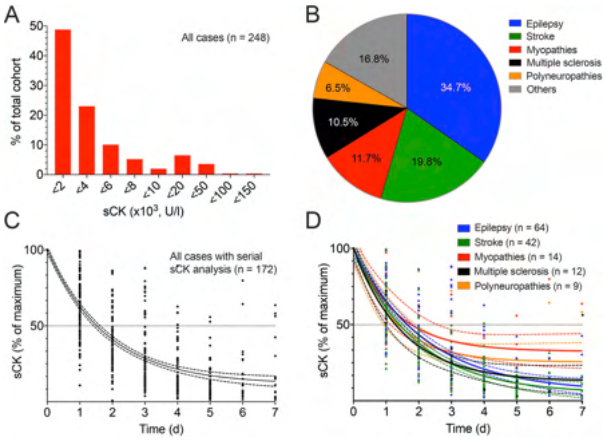

Figure 1. Distribution and time course of sCK activity in different neurological diseases associated with rhabdomyolysis

Table 2. Neurological diseases associated with rhabdomyolysis

Neurological diseases accounting for 5% of the cohort	≥ N
Epilepsy	86
Stroke	49
Cerebral ischemia	41
Intracranial hemorrhage	8
Myopathies	29
Hereditary myopathy	5
Idiopathic inflammatory myopathy	5
Endocrine myopathies	4
Other myopathies	15
Multiple sclerosis	26
Polyneuropathies	16
Guillain-Barré syndrome	3
CIDP	2
MMN	1
PNP associated with MGUS	1
Diabetic PNP	1
Alcoholic PNP	1
Unspecific (axonal) PNP	7
Neurological diseases accounting for 5% of the cohort	**< N**
Radiculopathy/spinal disc herniation	8
Parkinson's disease	4
Amyotrophic lateral sclerosis	3
Encephalitis	3
Neuromyelitis optica	3
Vascular myelopathy	2
Myasthenia gravis	1
Brachial neuritis	1
Traumatic brachial plexus injury	1
Post-polio syndrome	1
Stiff-person syndrome	1
Idiopathic intracranial hypertension	1
Cavernoma	1
Fibromyalgia	1
Dystonia	1
Narcolepsy	1
Unknown	9

CIDP, Chronic inflammatory demyelinating polyneuropathy; MGUS, Monoclonal gammopathy of undetermined significance; MMN, Multifocal motor neuropathy; PNP, Polyneuropathy.

Neurological diseases associated with rhabdomyolysis

	Number of individual cases treated at a tertiary neurological center between 2013-2017						Incidence/1,000 person-years (95% CI)
	2013	2014	2015	2016	2017	2013-2017	
Myopathies[1]	149	112	117	126	118	622	49.8 (32.3-67.4)
+ rhabdomyolysis	7	8	6	7	3	31	
Epilepsy[2]	1,265	1,032	776	825	930	4,828	16.4 (12.8-20.0)
+ rhabdomyolysis	7	12	27	17	16	79	
Stroke[3]	896	747	679	652	730	3,704	11.9 (8.4-15.4)
+ rhabdomyolysis	2	12	10	11	9	44	
Polyneuropathies[4]	732	450	367	302	380	2,231	6.7 (3.3-10.1)
+ rhabdomyolysis	0	6	2	4	3	15	
Multiple sclerosis[5]	1,012	858	835	914	972	4,591	4.1 (2.3-6.0)
+ rhabdomyolysis	1	2	5	6	5	19	

Table 4. Incidence of rhabdomyolysis in different neurological disease entities

[1] Myopathies included the ICD-10 codes G71.x (Primary disorders of muscles), G72.x (Other myopathies), M33.x (Dermatopolymyositis), M60.x (Myositis), M62.x (Other disorders of muscle) and M63.x (Disorders of muscle in diseases classified elsewhere). [2] Epilepsy included the ICD-10 codes G40.x (Epilepsy), G41.x (Status epilepticus) and R56.x (Convulsions, not elsewhere classified). [3] Stroke included the ICD-10 codes I61.x (Intracerebral hemorrhage), I62.x (Other nontraumatic intracranial hemorrhage), I63.x (Cerebral infarction), I64.x (Stroke, not specified as hemorrhage or infarction), I67.x (Other cerebrovascular disease), G45.x (Transient cerebral ischemic attacks and related syndromes) and G46.x (Vascular syndromes of brain in cerebrovascular disease). [4] Polyneuropathies included the ICD-10 codes G56.x (Mononeuropathies of upper limb), G57.x (Mononeuropathies of lower limb), G60.x (Hereditary and idiopathic neuropathy), G61.x (Inflammatory polyneuropathy), G62.x (Other polyneuropathies) and G63.x (Polyneuropathy in diseases classified elsewhere). [5] Multiple sclerosis included the ICD-10 codes G35 (Multiple sclerosis) and G37.x (Other demyelinating diseases of central nervous system).

Incidence of rhabdomyolysis in different neurological disease entities

Conclusion: Rhabdomyolysis occurs in a broad range of neurological entities but is usually associated with a favorable prognosis rarely resulting in AKI and death.
Disclosure: All listed authors report no disclosures.

EPR-184

Apitegromab, an Investigational Anti-proMyostatin Monoclonal Antibody for Spinal Muscular Atrophy: Phase 2 Results

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Background and aims: Apitegromab (SRK-015) is an investigational fully human, high-affinity anti-pro/latent myostatin monoclonal antibody that binds to human pro- and latent forms of myostatin and inhibits the tolloid-mediated proteolysis step for myostatin activation in vitro. Apitegromab is being developed for treating SMA.
Methods: Subjects with Types 2 and 3 SMA received apitegromab with or without an approved SMN upregulator (nusinersen). Primary objectives were to assess safety and tolerability of IV apitegromab infusions every four weeks and measure motor function changes after 52 weeks, assessed by mean change in Hammersmith Scale (RHS) scores. Secondary objectives were characterization of pharmacokinetics and pharmacodynamics of low- (2mg/kg) and high-dose (20mg/kg) apitegromab, immunogenicity and exploratory motor function measures.
Results: The planned 6-month interim analysis showed Cohort 1 subjects (ambulatory Type 3, n=23) who received apitegromab (20mg/kg) monotherapy or as adjunctive treatment to nusinersen, had a pooled mean change in baseline RHS scores of 0.5 (-1.1, 2.2). Cohorts 2 (n=14) and 3 (n=18) included Type 2 and non-ambulatory Type 3 subjects who received apitegromab (Cohort 2, 20mg/kg; Cohort 3, 2mg/kg and 20mg/kg) as adjunctive therapy to nusinersen treatment. The mean change in baseline Hammersmith Functional Motor Scale Expanded scores was 1.4 (0.1, 2.7) in Cohort 2, 2.4 (-0.9, 5.8) in low-dose Cohort 3 group, and 5.6 (2.5, 8.7) in high-dose Cohort 3 group.
Conclusion: The TOPAZ interim analysis results provide support for apitegromab as a potential treatment to improve motor function in SMA patients. Phase 2 topline data will be presented.
Disclosure: This study was sponsored by Scholar Rock, Inc.

EPR-185

Ocular myositis as a rare extraintestinal manifestation of Crohn's disease

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Background and aims: Ocular myositis, an autoimmune myopathy of the external eye muscles, may be idiopathic or associated with multisystem inflammatory disorders such as systemic lupus erythematosus, sarcoid or inflammatory bowel disease (IBD). Clinically, it is characterized by acute onset periorbital pain, painful eye movements and diplopia. The diagnosis is confirmed by contrast-enhanced orbital MRI. Steroid treatment leads to remission in 90% of patients. Immunosuppressants such as azathioprine, methotrexate or TNF-alpha blockers may be used in patients with refractory disease.
Methods: A 30-year-old patient with Crohn´s disease on symptomatic treatment developed recurrent erythematous painful swellings of her left eye with conjunctival irritation. Vision and fundoscopy were normal, but contrast-enhanced MRI of the orbit showed retrobulbar edema and enhancement of the left superior rectus muscle suggesting ocular myositis.
Results: The patient received prednisolone adjusted to body weight for eight days with subsequent tapering. At a daily dose of 10mg prednisolone, she developed a relapse which subsided partially when the dose was increased to 100mg per day. After tapering to 32.5mg she presented with residual symptoms which prompted us to escalate the treatment by adding methotrexate. This resulted in complete regression of all symptoms and normalization of the MRI. Because of persisting gastrointestinal symptoms, however, immunosuppression had to be switched to adalimumab.
Conclusion: To date, only few case reports of ocular myositis as an extraintestinal manifestation of IBD have been published. Because of its corticosteroid responsiveness, ocular myositis should always be considered in patients with IBD and ophthalmological symptoms.
Disclosure: Nothing to disclose.

EPR-186

The TREAT NMD LGMD Global Registry development

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Background and aims: The current Limb Girdle Muscular Dystrophy (LGMD) registry landscape is fragmented and there is no universal consensus on a dataset that multiple registries have agreed to collect. The acceleration of therapeutic development, the potential need for clinical trial development and ultimately the need for post market surveillance, require collaboration and consensus on a dataset for LGMD registries. The objective of this project is to establish the LGMD global registry network and reach consensus on a feasible LGMD dataset.

Methods: A working group (WG), including different stakeholders (clinical experts, patient representatives, registry curators and pharmaceutical company representatives), has been established. The dataset was developed through a series of four virtual meetings. Based on other TREAT-NMD dataset experiences, a consensus building process was applied to identify the purpose of the LGMD dataset and assess its feasibility.

Results: The WG agreed on three main objectives for the LGMD dataset: 1) Clinical characterization of the diseases, 2) Longitudinal data collection, 3) Recruitment and feasibility of clinical trial. 49 items have been agreed upon and included in the Dataset, covering from diagnosis, disease onset, clinical presentation, patient report and clinical outcome measures and treatment.

Conclusion: TREAT-NMD, through its network of registries, stakeholders, and partners, is ideally placed to drive forward the development of a unified dataset for LGMD registries, by pulling together Key Opinion Leaders, ensuring stakeholder collaboration, and encouraging partnership engagement. TREAT-NMD has experience and a proven track record of similar initiatives, where the outputs have led to cohesion and standardization in data collection.

Disclosure: The authors do not have relevant disclosures

EPR-187

Genotype-related respiratory progression in Duchenne Muscular Dystrophy – multicentre international study

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Background and aims: Mutations amenable to skipping of specific exons have been associated with different motor progression in Duchenne Muscular Dystrophy (DMD). Less is known about their association with long-term respiratory function. We aimed to investigate the features of respiratory progression in four DMD genotypes relevant for exon skipping strategies.

Methods: Retrospective longitudinal study including DMD children followed by UK North Star network and international AFM network centres (May 2003–October 2020). We included boys amenable to skip exons 44, 45, 51 or 53, older than five years and ambulant at 1st recorded visit. Patients corticosteroids naïve or enrolled in interventional clinical trials were excluded. The progression of respiratory function (forced vital capacity%, FVC% and absolute FVC) was compared across the four subgroups (skip44, skip45, skip51, skip53).

Results: We included 142 boys. Mean(SD) age at 1st visit was 8.6(2.5) years. Median follow-up was 3(0.3–8.3) years (Table 1). In skip45 and skip51 FVC% started declining immediately at five years from a maximum value of 97.5% and 110.6% respectively. In skip44 and skip53 FVC% peaked at 8.7 and 8.5 years to lower values of 89.8% and 89.4%. From the age of nine years FVC% linearly declined in all genotypes (Fig 1). Exon44 had the slowest (2.7%/year) and skip51 the fastest (5.9%/year) annual FVC% decline. Absolute FVC progressively increased in skip44, skip45, skip 51. In skip53 it plateaued between 10–14 years then declined (Fig 2).

	Exon 44 (N=35)	Exon 45 (N=37)	Exon 51 (N=46) *	Exon 53 (N=29) *
Median follow up [min,max]	2.9 (0.5, 6.7)	2.5 (0.3, 8.0)	3.5 (0.4, 8.3)	3.4 (0.5, 8.3)
Mean age last visit [±SD]	11.2 (3.1)	11.1 (3.4)	13.1 (2.9)	11.7 (3.7)
Median age at LoA [IQR]	16.8 (11.9, 16.8)	14.1 (11.7, 15.9)	13.4(11.7, 16.6)	13.6 (11.4, 15.8)

Table 1. Patients population

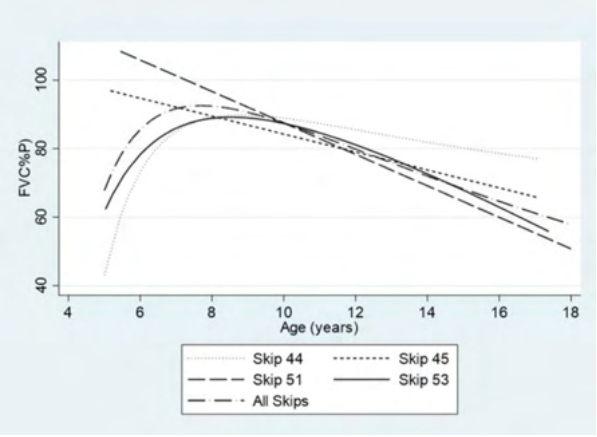

Figure 1. Progression of FVC% across DMD genotypes (skip44, skip45, skip51 and 53)

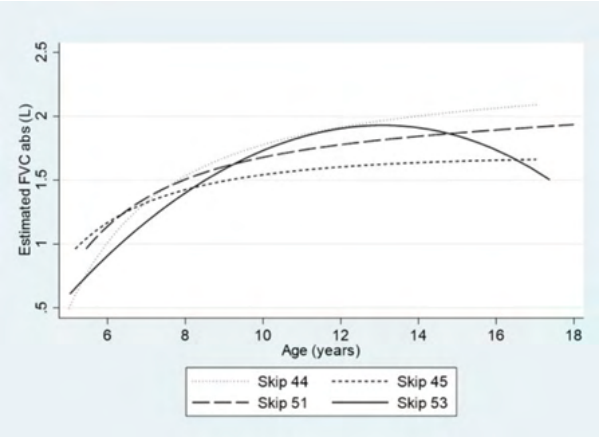

Figure 2. Progression of FVC% across DMD genotypes (skip44, skip45, skip51 and 53)

Conclusion: The identification of genotype-related respiratory progression in DMD boys is valuable for prognosis and for evaluation of exon skipping treatments.

Disclosure: Nothing to disclose.

EPR-188

Myasthenia gravis from the patient's perspective: Fatigue is bothersome and its improvement an important treatment goal

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Background and aims: Patients' perspectives of the most bothersome symptoms of generalised myasthenia gravis (gMG) and their treatment have not been systematically characterised. This study aimed to identify these symptoms, their impact on daily life, and patients' treatment goals.

Methods: Qualitative research was conducted through semi-structured telephone interviews (~75min) with 28 adult patients with gMG in the US currently receiving at least one gMG treatment. Transcripts were analysed to identify important concepts and themes, without imposing an a priori theory.

Results: Patient characteristics are in Table 1. Fatigue, blurry/double vision, difficulty swallowing, and breathing problems were reported as the most bothersome gMG symptoms (Table 2). Patients distinguished between muscle weakness (reported by 86%) and physical fatigue (89%), and further identified mental fatigue (46%) as a distinct symptom. 27 (96%) patients reported fluctuating symptoms, particularly fatigue and weakness. 26 (93%) patients reported onset/worsening of fatigue with usual/normal activities or over the course of the day (fatigability). 25 (89%) patients reported the need to plan, modify, or cancel activities because of symptoms; the majority of these (23/25, 92%) did so because of fatigue, fatigability, or muscle weakness. Improvement in fatigue or weakness was the most common treatment goal cited by patients (39%).

	Patients (N=28)
Female, n (%)	18 (64)
White, n (%)	26 (93)
Age group, n (%)	
18–34 years	6 (21)
35–50 years	9 (32)
51–69 years	9 (32)
≥70 years	4 (14)
MG-ADL total score, mean ± SD	5.54 ± 3.55
Education level, n (%)	
High school diploma/GED	4 (14)
Some college/no degree	7 (25)
Associate degree or higher	17 (61)

GED, general educational development tests; MG-ADL, Myasthenia Gravis-Activities of Daily Living.

Table 1. Participant demographics and characteristics

	Fatigue	Blurry vision	Difficulty swallowing	Breathing problems
Sex, n (%)				
Female	18 (100)	16 (89)	16 (89)	18 (100)
Male	10 (100)	9 (90)	10 (100)	9 (90)
Age group, n (%)				
18–34 years	6 (100)	6 (100)	5 (83)	6 (100)
35–50 years	9 (100)	8 (89)	9 (100)	9 (100)
51–69 years	9 (100)	7 (78)	8 (89)	8 (89)
≥70 years	4 (100)	4 (100)	4 (100)	4 (100)

Table 2. Most bothersome symptoms, by patients' sex and age (N=28)

Conclusion: Patients with gMG reported several bothersome symptoms, frequently and spontaneously describing/highlighting fatigue and weakness that necessitated adaptations and restrictions to their daily activities. The negative impact of fatigue and weakness on patients' lives was underscored by the fact that patients considered amelioration of these symptoms as their primary treatment goal.

Disclosure: Research funding for this study was provided by Alexion Pharmaceuticals.

EPR-189

NEO-EXT: Skeletal Muscle % Fat in Late-Onset Pompe Disease After Long-Term Avalglucosidase Alfa (3-point Dixon MRI)

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Background and aims: Long-term avalglucosidase alfa effects on skeletal muscle fat fraction, a muscle degeneration biomarker, were assessed using magnetic resonance imaging (MRI) in participants with late-onset Pompe disease (LOPD) during NEO-EXT (NCT02032524), a NEO1 (NCT01898364) extension.

Methods: NEO1 participants, treatment-naïve (Naïve) or receiving alglucosidase alfa for ≥9 months (Switch), received avalglucosidase alfa (5, 10, or 20mg/kg qow) for six months. Those subsequently entering NEO-EXT continued their NEO1 dose until 2016, when all received 20mg/kg qow thereafter. Quantitative MRI, 3-point Dixon images were used to measure skeletal muscle fat fraction at NEO1 enrollment and the impact of avalglucosidase alfa on changes in fat infiltration after 2- and 4-years' treatment.

Results: NEO1 enrolled 24 participants; 19 entered NEO-EXT. At NEO1 enrollment, skeletal muscle % fat fraction was determined in the context of a clinical evaluation and found to be consistent with previous LOPD natural history. Overall, there were minimal changes in % fat fraction in NEO1. Changes from Week 27 for quadriceps and hamstring muscle % fat fraction at Year 2 and Year 4 are shown in the Table. Overall, during NEO-EXT, % fat fractions in quadriceps and hamstring were generally stable for the study duration in most participants.

	% fat fraction, mean (SD) [median (range)] at Week 27 (NEO-EXT baseline)		Change in % fat fraction from Week 27 to Year 2 (Weeks 104/130), mean (SD)		Change in % fat fraction from Week 27 to Year 4 (Weeks 208/234), mean (SD)	
	Naïve Group	Switch Group	Naïve Group	Switch Group	Naïve Group	Switch Group
Participants, n	6	8	5	8	2	4
Quadriceps	9.9 (3.4) [9.5 (6–15)]	13.0 (6.8) [12.1 (6–24)]	1.15 (1.38)	0.88 (2.87)	1.45 (1.85)	0.30 (1.24)
Hamstring	38.3 (26.5) [34.5 (11–73)]	26.6 (19.1) [21.5 (10–68)]	1.88 (4.85)	1.14 (3.24)	5.29 (3.23)	−0.21 (7.08)
SD, standard deviation						

Table Percent fat fraction in quadriceps and hamstring muscle at Week 27 (NEO-EXT baseline) and changes in % fat fraction from Week 27 to Years 2 and 4

Conclusion: The data suggest that avalglucosidase alfa may assist in muscle preservation, contrasting with worsening fatty replacement observed in untreated natural history of LOPD and in some patients receiving alglucosidase alfa. 3-point Dixon could be potentially useful in long-term clinical trials of patients with LOPD, in which fatty infiltration slowly progresses over time.

Disclosure: Funding: Sanofi Genzyme

EPR-190

Safety, Beta-Sarcoglycan Expression and Functional Outcomes From rAAVrh74.MHCK7.SGCB Systemic Gene Transfer in LGMD2E/R4

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Background and aims: Limb-girdle muscular dystrophy type 2E/R4 (LGMD2E/R4), caused by loss-of-function mutations in the beta-sarcoglycan (SGCB) gene, leads to progressive muscle weakness and cardiac involvement. Here, we report initial findings of a Phase 1/2 clinical gene transfer trial of a self-complementary rAAVrh74.MHCK7.hSGCB construct (SRP-9003) designed to restore functional SGCB.

Methods: In this ongoing, first-in-human, single-centre, open-label, Phase 1/2 study (NCT03652259), patients with LGMD2E/R4 received a single IV infusion of 1.85x10^13vg/kg (Cohort 1; n=3) or 7.41x10^13vg/kg (Cohort 2; n=3). Eligibility: age 415 years, SGCB gene mutation (both alleles), negative for rAAVrh74 antibodies, >40% on 100-meter timed test. All patients received prednisone 1mg/kg/day one day before treatment (tapering after 30–60 days). Primary endpoint was safety, secondary endpoint was SGCB expression at Week 8, and other endpoints included creatine kinase (CK) decrease and functional tests.

Results: Systemic administration of SRP-9003 is well tolerated with no unexpected immunologic responses observed. There were no decreases in platelet counts outside normal range, and no clinical sequelae associated with complement activation. Results show efficient transduction and robust SGCB protein expression in all patients post infusion, leading to sarcoglycan complex reconstitution and CK reduction. six months after SRP-9003 infusion, patients from both cohorts experienced functional measure improvements versus baseline. For Cohort 1, data up to 18 months post infusion are available and demonstrate improvements in functional tests maintained over baseline.

Conclusion: These data suggest long-term efficacy of SRP-9003 gene-transfer therapy, supporting advancement of the clinical development program.

Disclosure: LRRK, ERP, SL, DAG, ASM, and JR: Current or former employees of Sarepta Therapeutics, Inc. KJL, KC, NFM, MAI, and LPL: No conflicts to disclose. JRM: Travel support from Sarepta Therapeutics, Inc. Products are investigational only.

ePresentations

Sunday, June 20 2021
Ageing and dementia 4

EPR-191

Validation of the 2017 Euro-CJD Diagnostic Criteria for Sporadic Creutzfeldt-Jakob Disease

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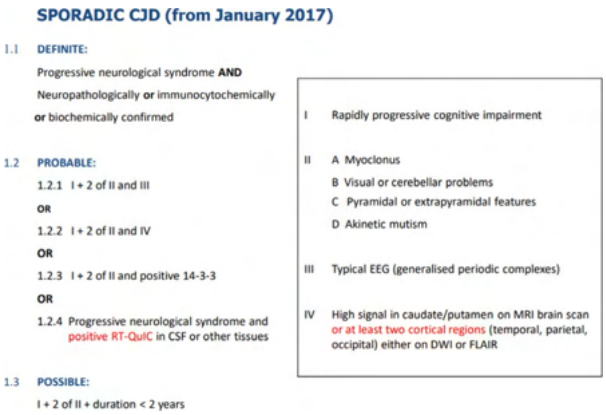
Background and aims: Sporadic Creutzfeldt-Jakob disease (sCJD) is the commonest form of CJD, a universally fatal and rapidly progressive human prion disease. sCJD typically presents with rapidly progressive dementia but can have diverse manifestations. Many conditions can 'mimic' sCJD, including treatable diseases. The diagnosis can be challenging. Diagnostic criteria weeevised in 2017 to include the real-time quaking-induced conversion (RT-QuIC) assay and cortical ribboning on magnetic resonance imaging (MRI). The aim of this study is to validate the diagnostic criteria, with the secondary aim of evaluating its impact on case classification during life.



Diagnostic criteria for sCJD; 2017 revisions in red

Methods: All deceased subjects with post-mortem (PM)-confirmed sCJD between 2017–2019 were included from the national registries of the UK, France, Germany and Italy. A control group investigated for sCJD with an alternative diagnosis at PM was included. Diagnostic test outcomes were recorded. Subgroup analysis was performed assessing test outcomes according to prion protein gene (PRNP) codon 129 status. Subjects were classified during life according to the previous and updated criteria to assess the impact on ascertainment.

Results: 501 sCJD cases and 146 non-cases were included. sCJD subjects were younger (mean 68.9 vs 72.7 years, p<0.001). RT-QuIC was 91.6% sensitive and 100% specific. MRI was the second most sensitive (86.8%) and specific (91.9%) investigation. Codon 129 had a significant impact on MRI changes in sCJD (p<0.001). Revised criteria increased in-life sCJD diagnosis by 22.4%.

	% fat fraction, mean (SD) [median (range)] at Week 27 (NEO-EXT baseline)		Change in % fat fraction from Week 27 to Year 2 (Weeks 104/130), mean (SD)		Change in % fat fraction from Week 27 to Year 4 (Weeks 208/234), mean (SD)	
	Naïve Group	Switch Group	Naïve Group	Switch Group	Naïve Group	Switch Group
Participants, n	6	8	5	8	2	4
Quadriceps	9.9 (3.4) [9.5 (6–15)]	13.0 (6.8) [12.1 (6–24)]	1.15 (1.38)	0.88 (2.87)	1.45 (1.85)	0.30 (1.24)
Hamstring	38.3 (26.5) [34.5 (11–73)]	26.6 (19.1) [21.5 (10–68)]	1.88 (4.85)	1.14 (3.24)	5.29 (3.23)	−0.21 (7.08)

SD, standard deviation

Demographics of study subjects

	Sporadic CJD (cases)	Non-CJD (controls)	*
Demographics			
Sex (M:F)	253:247	74:72	p=0.98
Mean age, years (SD)	68.9 (9.5)	72.7 (10.3)	**p<0.001**
Median duration, days (IQR)	118 (74.75-222.25)	85 (51.5-205.5)	**p=0.002**

*p value from X^2 test for sex, Student's t-test for age, Mann Whitney U test for duration
† CI = 95% confidence intervals

Investigation outcomes

Conclusion: The diagnostic criteria are highly sensitive and specific, particularly RT-QuIC, allowing effective differentiation of sCJD from potentially treatable mimics, and enhancing in-life sCJD diagnosis rates.

Disclosure: No conflicts of interest to declare

EPR-192

Multimodal evaluation of the melanopsin retinal ganglion cells system and circadian rhythms in Alzheimer's disease

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Background and aims: Melanopsin retinal ganglion cells (mRGCs) are deputed to circadian photoentrainment and pupillary light reflex (PLR) regulations. Circadian dysfunction is reported in Alzheimer's disease (AD) and contributes to dementia. Single-Nucleotide-Polymorphisms (SNPs) in clock genes have been associated to AD.

Methods: We included 29 mild-moderate AD and 26 matched controls and performed neuro-ophthalmological evaluation including optical coherence tomography (OCT), actigraphic recordings of rest-activity rhythms, chromatic pupillometry and brain functional MRI (fMRI) with light stimulation. 84 clock genes were analyzed by NGS and relevant SNPs validated in a larger cohort of AD (n=449) and controls (n=326).

Results: In AD disease duration was 3.9±2.8 years and MMSEc score 20.2±4.2. OCT showed a significant reduction of the infero-temporal GCL thickness (p=0.036) in AD. Actigraphy did not disclose significant differences for circadian parameters (IS, IV, RA). However, a subgroup of "circadian-impaired" AD was evident, and most of circadian parameters declined with aging. Pupillometry revealed a significant reduction of PLR peak amplitude in the rod protocol (p=0.006) significantly correlating with aging in AD. Brain fMRI documented the absence of significant responses in AD with sustained blue light stimulation at difference with controls. Genetic analysis in extended AD and control cohorts showed a significant association of the rs30127178 SNP in PER1 gene with AD.

Conclusion: These results demonstrate, by innovative multi-modal approach, that mRGC system in AD is affected by neurodegeneration. This can be envisaged as a possible biomarker also for conversion from MCI to AD with potential implication for light therapy as a counteracting measure for dementia.

Disclosure: This work was supported by the Italian Ministry of Health grant GR-2013-02358026 to CLM

EPR-193

Association between EEG features and CSF biomarkers in Mild Cognitive Impairment: a cross-sectional study

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Background and aims: Electroencephalographic analysis (EEG) could play a pivotal role as non-invasive and economically sustainable biomarker of conversion from Mild Cognitive Impairment (MCI) to Alzheimer´s Disease (AD). We aimed to assess the association between EEG characteristics of MCI patients, evaluated through a quantitative EEG analysis (qEEG), with CSF AD biomarkers, valuate the accuracy of qEEG in predicting an underlying AD pathology.

Methods: We included 21 MCI patients. All patients underwent neuropsychological tests, ApoE genotyping, CSF analysis of Amyloid Beta 42 (A42), A42/A40 ratio, total Tau (T-tau) and phosphorylated Tau (P-Tau), EEG and qEEG analysis.

Results: We found a direct correlation between parieto-occipital theta frequency proportion with A42, A42/A40 ratio, P-Tau, T-Tau, P-tau/A42 ratio, T-Tau/A42 ratio without significant differences in laterality. Patients with positive CSF AD profile had higher proportion of parieto-occipital theta frequencies. We calculated the index "Total PO Theta" as sum of left and right parieto-occipital theta relative power. Through a regression analysis we developed an equation to predict the probability of CSF positivity according to Total PO Theta. We found a cut-off value of 33.9% of Total PO Theta to identify with a very good accuracy MCI patients who had positive CSF AD biomarkers (ensitivity of 77.8% and a specificity of 75% for A42, 87.5% and 76.9% for P-Tau/A42).

Conclusion: Our data suggest that the Total PO Theta biomarker may constitute a valid, economic, non-invasive and easily accessible tool to predict the presence of an underlying AD pathology behind the MCI.

Disclosure: Nothing to disclose.

EPR-194

Levels of proinflammatory cytokines il-17 and il-23 in patients with Alzheimer's disease and mild cognitive impairment

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Background and aims: The levels of several cytokines are possible indicators of neuroinflammation in Alzheimer's disease (AD) which could contribute to the development of neurodegeneration. We aimed to study differences of interleukin (IL)-17 and IL-23 serum levels in patients with AD and mild neurocognitive disorder (NCD).
Methods: The study involved 45 patients with cognitive impairment (21 men, 24 women, mean age – 66.8±8.4), 14 (33.3%) of them has major NCD and meet to updated criteria for the diagnosis of Alzheimer's according to the NINDS-AIREN and 30 has mild NCD. Patients with mild NCD was divide to amnestic mild cognitive impairment (MCI) (aMCI) – nine (20.0%) and nonamnestic MCI (naMCI) – 21 (46.7%). Serum levels of IL-17 and IL-23 were measure by ELISA.
Results: Serum concentrations of IL-17 were significantly higher in AD compared with MCI (22.44±8.92 pg/ml vs 4.04±1.10 pg/ml; p=0.0065). No significant differences in serum concentration of IL-17 observed in aMCI and naMCI patients (p=0.6411). IL-23 level also was significant higher in AD patients (64.33±22.41 pg/ml vs 1.84±0.38pg/ml; p=0.0003). When compared patients with aMCI and naMCI significant differences in increase IL-23 (2.80±0.17 pg/ml vs 1.43±0.21 pg/ml; p=0.0004) in aMCI was found.
Conclusion: Our results suggest that in patients with AD interleukins levels significantly higher compare with mild NCD that reflect increase of inflammatory response. Significant differences between aMCI and naMCI groups was demonstrate for IL-23 that may be evidence of potential role of this interleukin as additional biomarkers for early predict of progression aMCI in AD.
Disclosure: Nothing to disclose.

EPR-195

White matter damages related to behavioural disinhibition assessed in semi-ecological context in frontotemporal dementia

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Background and aims: Behavioural variant frontotemporal dementia (bvFTD) is partly characterised by inhibition disorders. Neural correlates of disinhibition being poorly known, we aim to identify white matter bundles associated to behavioural disinhibition.
Methods: We assess behavioural disinhibition in a semi-ecological setting, noting occurrences of 19 behaviours – derived from clinical criteria of bvFTD – related to compulsivity, impulsivity or social disinhibition, in a population of 20 bvFTD and 20 healthy controls (HC). Subjects also undergo an MRI. In this study, diffusion tensor tractography (DTT) was used to investigate white matter changes in bvFTD patients compared to HC. DTI metrics – fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD) and radial diffusivity (RD) – are then correlated to behavioural disinhibition scores.
Results: This analysis was conducted on seven bvFTD patients and seven HC. Results show a significant decrease of FA in the cingulum, the forceps minor (FM) and the uncinate fasciculus (UF) in bvFTD patients. In addition, there is a significant increase of MD and RD in bvFTD patients in the FM and the UF, as well as a significant increase of RD in bvFTD patients in the cingulum. Among bvFTD patients, there is a tendency to associate compulsivity to a weaker integrity of the cingulum and the left UF while social disinhibition is correlated to alterations of the right UF.
Conclusion: The cingulum is already known to be impaired in obsessive-compulsive disorder and UF is related to behavioural and social disinhibition, which is consistent with our findings based on a semi-ecological assessment of behavioural disinhibition.
Disclosure: Nothing to disclose.

EPR-196

Cerebellar Atrophy in Sporadic Alzheimer's disease

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Background and aims: The role of the cerebellum in cognitive function has been extensively investigated in the last decades. Recent studies indicate that cerebellum may play a role in Alzheimer's disease (AD) pathogenesis. We performed voxel-based morphometry (VBM) to assess cerebellar atrophy in AD patients.
Methods: 15 patients with sporadic AD dementia and amnestic mild cognitive impairment (mean age 76.1±9.0 years, five males) and 10 healthy controls (65.6±11.3 years, four males) were included in the study. Disease duration ranged from 12 to 60 months. Notably, the patients had no clinical signs of cerebellar involvement. All participants underwent brain MRI using 3D-T1 MPR sequence. VBM was performed using SPM12. The VBM results were assessed by cluster analysis using the two-sample t-test with the whole brain voxel-wise comparison of gray matter volume between the studied groups (minimum cluster size 100 voxels, pFWE-corr <0.01).
Results: In addition to the expected relatively symmetric atrophy of the hippocampi, temporal lobes, insula, inferior areas of parietal lobes and superior frontal gyri, marked atrophy of the cerebellum was detected. The involvement of lateral superior areas of cerebellum hemispheres bilaterally with spreading to Crus I and II on the right hemisphere was shown (Figure 1).

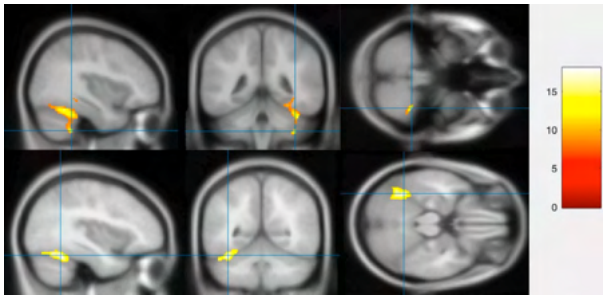

Figure 1. Localization of significant (pFWE-corr<0.01) GM volume decline in patients with AD compared to control group. Upper row: atrophy of the right cerebellar hemisphere. Lower row: atrophy of the left cerebellar hemisphere.

Conclusion: Our study shows that, even in the absence of clinical signs of cerebellar involvement, prominent cerebellar atrophy in sporadic AD may be seen, which supports the role of cerebellum in cognitive functions and provides further evidence of its possible role in AD pathogenesis.
Disclosure: Nothing to disclose.

EPR-197

Gender proportions in clinical trials for Alzheimer's disease: results from a systematic review and meta-analysis

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Background and aims: Alzheimer's disease (AD) exhibits a heterogeneity that likely influences clinical trials (CTs). As two-thirds of AD patients are women, gender presumably plays a role. No previous studies have examined gender ratios in CTs of experimental medications for AD.
Methods: We conducted a systematic review and meta-analysis utilizing clinicaltrials.gov, Pubmed, Google Scholar, and Scopus, examining published CTs for AD with over 100 participants testing efficacy of medications and herbal extracts. Of initial 1047 publications, 56 primary publications on AD dementia were analysed. We calculated the average percentage of women per trial, examined temporal trends and potential influencing covariates. In a posthoc analysis, we examined the influence of the proportion (%) of participants who withdrew from the trial due to an adverse event (AE).
Results: The 56 trials examining AD dementia patients included 59.1% women. The proportion of women was significantly higher in CTs of approved than in experimental medications (67.3% v. 57.9% women, p<0.001), in trials with lower mean baseline MMSE (63.3% v. 55.5%, p<0.001) and in trials in Asia compared to North American trials (65.3% v. 54.5%, p<0.001). Age, trial phase, trial duration, or % of withdrawals due to AEs showed no association with the proportion of women. No significant temporal trend was observed.
Conclusion: The proportion of women in clinical trials for AD, especially experimental medications, does not reflect the current prevalence of the disease. This could suggest potential barriers to AD CT participation for women. Preliminary results do not suggest an influence of withdrawal due to AEs or trial duration.
Disclosure: Supported by GAUK 436119 at Charles University, 2.LF. MTF: unrelated fees from Eli Lilly. ASC: employed at Biogen. FCQ: employed at Roche Diagnostics. H.K.: employed at Novartis. E.S.: unrelated fees from Bayer and Novartis.

EPR-198

A cohort study on dementia and the risk of periodontitis over a 16-year follow-up

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Background and aims: Dementia has been proposed to be comorbid with periodontitis in cross-sectional studies. We identified the effect of dementia on periodontitis in this longitudinal study.
Methods: 8,640 dementia patients without prior periodontitis were recruited in this cohort study using data from the Longitudinal Health Insurance Dataset, for which 8,640 individuals without dementia history were selected as matched-controls. With propensity score matching, factors including cardiovascular diseases, diabetes, brain trauma, oral hygiene awareness, and socioeconomic factors, were controlled. Cox proportional hazard models were developed to estimate the risk of periodontitis. A log-rank test was derived to assess the time-dependent effect of dementia on periodontitis. Subgroup analyses on age stratification were included.
Results: 2,670 dementia patients developed periodontitis. The relative risk of periodontitis in dementia patients was significantly higher than non-dementia controls (1.825, 95% CI=1,715–1,942). Cox proportional hazard models showed that dementia patients were more likely to have periodontitis than non-dementia individuals (hazard ratio=1,915, 95% CI=1,766–2,077, p-value<0.0001). The observed effect of dementia on periodontitis was time-dependent (log-rank test p-value p<0.0001). Moreover, the risks of periodontitis in dementia patients were age-dependent (p-values for all ages<0.0001), which younger dementia patients were more likely to develop periodontitis.
Conclusion: These findings implied a possible causal relationship between dementia and periodontitis. That is, dementia was associated with higher risks of periodontitis. The effect of dementia on periodontitis was independent of systemic confounding factors and was age-dependent. Referrals to periodontists or general dentists are recommended for dementia patients.
Disclosure: N/A

Cognitive neurology/neuropsychology 1

EPR-199

Gamma tACS over the precuneus in Alzheimer's disease: a randomized, double-blind, sham-controlled, cross-over trial

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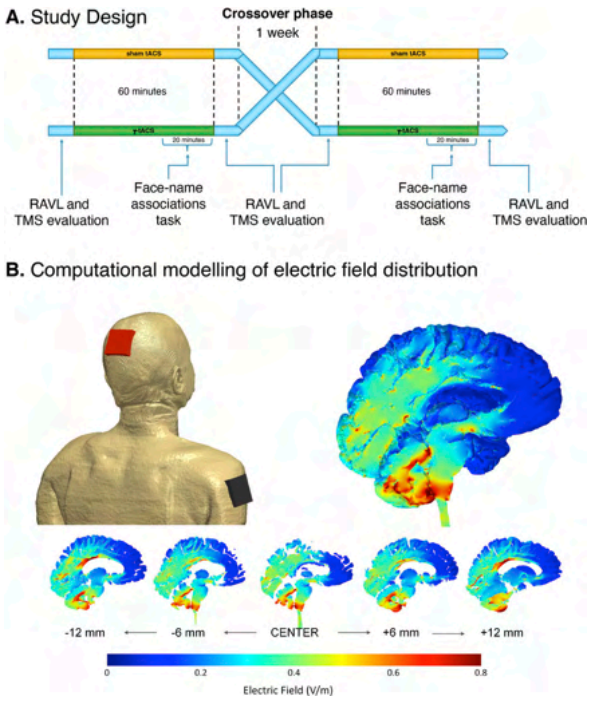
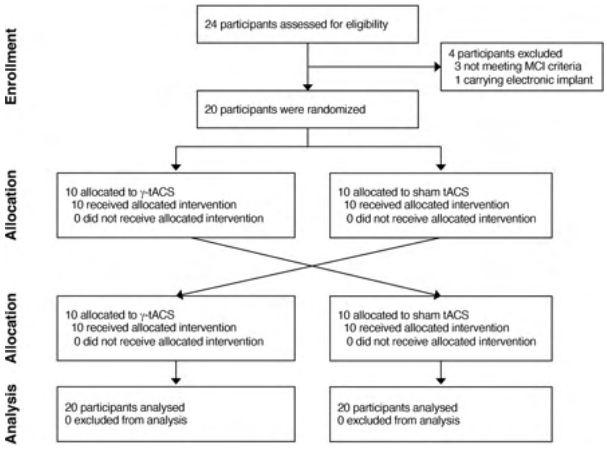
Background and aims: The restoration of gamma oscillations by neural entrainment in animal models of Alzheimer's disease have shown to induce a remarkable decrease in the pathological burden of amyloid and tau via increased microglial activity, resulting in an improvement of cognitive performances. We aimed to assess whether non-invasive brain stimulation with transcranial alternating current stimulation at gamma frequency (gamma-tACS) can improve memory and modulate cholinergic transmission in mild cognitive impairment due to Alzheimer's disease (MCI-AD).

Methods: In this randomized, double-blind, sham controlled, cross-over pilot study, participants were assigned to treatment with gamma-tACS targeting the precuneus or sham tACS. Each subject underwent a clinical evaluation including assessment of episodic memory pre- and post-gamma-tACS or sham stimulation. Indirect measures of cholinergic neurotransmission evaluated using transcranial magnetic stimulation (TMS) pre- and post-gamma-tACS or sham tACS were evaluated.

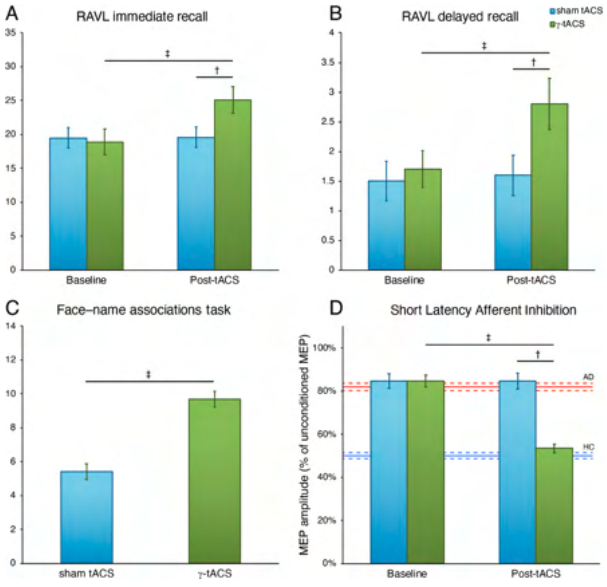


A) Study design and B) computational modelling of electric field distribution.



Flowchart of study patients.

Results: 20 MCI-AD patients completed the study. We observed a significant improvement at the Rey auditory verbal learning (RAVL) test total recall (5.7 [95% CI, 4.0 to 7.4], p<0.001) and delayed recall scores (1.3 [95% CI, 0.4 to 2.1], p=0.007) after gamma-tACS but not after sham tACS. Face-name associations scores improved during gamma-tACS (4.3 [95% CI, 2.8 to 5.8], p<0.001) but not after sham tACS. Short latency afferent inhibition, an indirect measure of cholinergic transmission evaluated with TMS, increased only after gamma-tACS (0.31 [95% CI, 0.24 to 0.38], p<0.001) but not after sham tACS.



A) RAVL total recall, B) RAVL long delayed recall, C) FNAT scores and D) SAI measures before and after gamma-tACS over the precuneus or sham stimulation

Conclusion: Gamma-tACS targeting the precuneus showed a significant improvement of memory performances, along with restoration of intracortical connectivity measures of cholinergic neurotransmission, compared to sham tACS.

Disclosure: No disclosures. relevant to the study

EPR-200

Motor sequence learning in patients with limb apraxia: Effects of long-term training

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Background and aims: Our study aims at investigating explicit motor learning in apractic stroke patients. In particular, we addressed the ability of apractic patients to learn and to store new sequential finger movements long-term across multiple sessions.
Methods: 12 stroke patients with upper limb apraxia in its chronic state participated in a three weeks' multiple session training. Each patient performed a standardized explicit finger sequence learning task, which is a well-established paradigm to investigate motor learning and memory processes. Motor sequence performance was measured in terms of speed and accuracy.
Results: Patients improved task performance in terms of speed and accuracy across sessions. They showed a noticeable reduction in the mean time needed to perform a correct sequence, and of the number of erroneous sequences. Accuracy fluctuated highly between the first and the last training session, but improved numerically over the course of the training. We found also some improvements in apraxia scores.
Conclusion: Patients with limb apraxia were able to learn a novel motor sequence across a long term training protocol, thus, revealing preserved capacity for long term formation of motor memories and most probably for some motor planing. We found also some transfer to amelioration of apraxia symptoms.
Disclosure: The authors do not have any financial nor any other disclosures.

EPR-201

A five-year longitudinal follow-up of cognitiveperformance in different MS subtypes

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Background and aims: Several cross-sectional studies report cognitive decline in multiple sclerosis (MS), but longitudinal studies with sufficiently long-term follow-up are still lacking. Our aim was to investigate the cognitive 5-year course of patients with relapsing–remitting (RR), secondary progressive (SP), primary progressive (PP) multiple sclerosis, and patients with clinically isolated syndrome (CIS) relative to control participants in the Greek population.
Methods: RR patients (n=80), SP patients (n=42), PP patients (n=28), CIS patients (n=48), and healthy control subjects (n=50) were assessed by the Brief Repeatable Battery of Neuropsychological Tests (BRBN), stroop and trail making test.
Results: A total of 152 patients (61,2%) were defined as cognitively impaired at baseline on at least one test, and 93 (37.9%) were defined as impaired at follow-up at 72 months. Logistic regression models showed that each standard deviation slower baseline information processing speed (IPS) or decline in IPS over time increased the likelihood of incident dementia (odds ratios 1.51, 95% confidence interval [CI] 1.31–1.98; and 2.44, 95% CI 2.12–3.14, respectively). Mixed-effects models revealed statistical interactions of time with dementia on change in verbal learning /memory capacity and executive functions (EF) of CIS and RRMS patients, such that those who developed dementia showed accelerated decline.
Conclusion: In this largest longitudinal study, memory and EF deficits seem to be more frequent in the CIS and RRMS progression, although IPS seems to progress slowly. The pattern of cognitive dysfunction in patients with CIS and RRMS is similar with relative sparing of verbal learning
Disclosure: Nothing to disclosure

EPR-202

The rise and fall of the terms describing functional neurological disorders in the past 60 years medical literature

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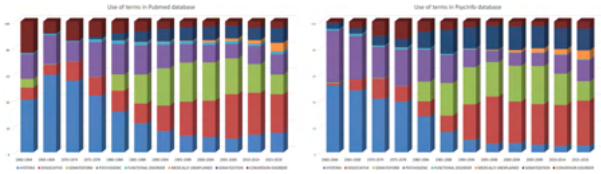
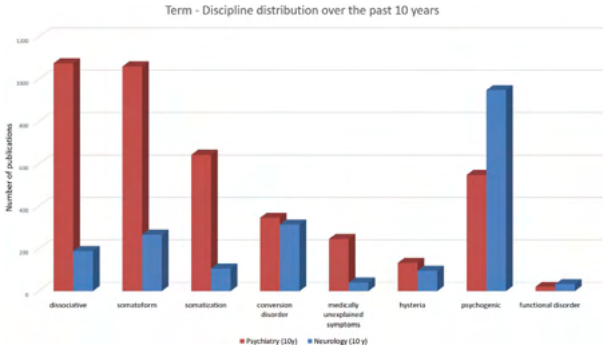
Background and aims: The choice of terms describing functional neurological disorders (FND) varied across time. They reflected dominant etiological paradigms or aimed at being neutral.

Methods: To conduct a bibliometric analysis among published articles using different terms across a 60-year-long period (1960–2020) in two major databases. Eight terms were retrieved: "Psychogenic", "Somatization", "Somatoform", "Medically unexplained symptoms" (MUS), "Hysteria", "Conversion disorder" (CD), "Functional disorder" (FD) and "Dissociative". Use rates in title, abstract, keyword or MeSH were collected over successive 5-year periods in the Pubmed and Psycinfo databases. Proportional distribution, respective associations, disciplinary fields (Neurology, Psychiatry) and term impact were calculated.

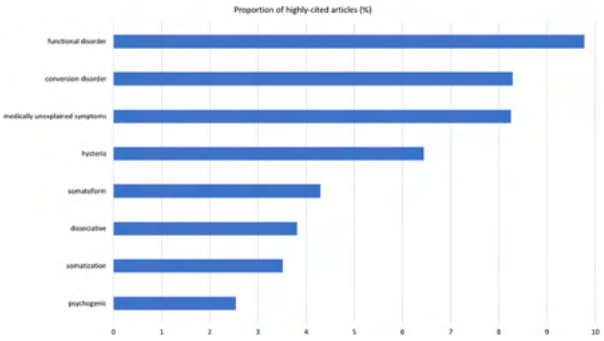
Results: "Hysteria" occupied 40–51% of FND-related publications until the 1980s, then became less present (4.8–18%). Over the last 10 years the term "dissociative" took the lead (30–34%). Three distinct evolutionary profiles of use were detected, reflecting the influence of epistemological views. "FD" and "psychogenic" were preferentially linked with "neurology", whereas "somatization", "somatoform" and "dissociative" were more associated with "psychiatry". The strongest between-terms association was observed with "hysteria" and "CD", appearing simultaneously in 25% of the results. The most influential term was found to be "FD" with a proportion of highly-cited articles of 10%, while this proportion was of only 2.5% concerning "psychogenic".



Terms distribution



Terms-discipline association



Proportion of highly-cited articles

Conclusion: The changing rate of use of FND-related terms over time reflects the different explanatory paradigms, some becoming obsolete (Hysteria), others persisting (Psychogenic) or showing some development (Dissociative, MUS). However, neutral terms, free from any explanatory perspective, like MUS, are not frequently used. A precise, explanatory and non-offensive term remains yet to be found.

Disclosure: Nothing to disclose.

EPR-203

Can we do more with neuropsychology? Behavioural Variant Frontotemporal Dementia and early Alzheimer's disease.

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Background and aims: The Index of sensitivity of cueing (ISC), an index of the Free and Cued Selective Reminding test (FCSRT), and the Semantic Index (SI) [1], obtained by the ratio between semantic and phonemic verbal fluencies, have been indicated as useful indexes to distinguish between Behavioural Variant Frontotemporal Dementia (bvFTD) and early Alzheimer's disease (AD) [2]. Our aim is to evaluate their accuracy, alone and in combination.

Methods: 34 bv-FTD (MMSE score: 25.32±2.96; age: 74.9±6.5; education: 8.2±4.1; gender 13M/21F) and 125 early AD patients (MMSE score:25.38±2.77; age:75.5±6.1; education:9.7±4.3; gender 52M/73F), who underwent neurological examination and neuropsychological evaluation were included in the study. The diagnosis was confirmed by neuroimaging with MRI, F-18 fluorodeoxyglucose Positron Emission Tomography (FDG-PET), and clinical follow up of at least two years.

Results: Age, education, gender and MMSE score did not significantly differ between groups (Tab.1). Areas under the Receiver Operating Characteristic (ROC) curves (AUC) were for ISC=0.664 (sensitivity=0.647; specificity=0.688; accuracy=0.679) and for SI=0.676 (sensitivity=0.5; specificity=0.816; accuracy=0.748). AUC combining the two indexes (binary logistic regression) was 0.710 (sensitivity=0.618; specificity=0.808; accuracy=0.767). Comparisons between the three AUC were not significant (Fig.1, Tab.2).

Table 1. Demographical and clinical characteristics of the population

	AD (n = 125)	bvFTD (n = 34)	F	Sig.
Age	75.5 ± 6.1	74.9 ± 6.5	0.304	0.582
Education	9.7 ± 4.3	8.2 ± 4.1	3.029	0.084
Gender*	52M/73F	13M/21F	0.125	0.723
MMSE	25.38 ± 2.77	25.32 ± 2.96	0.009	0.923

** In this case, the comparison between groups was carried out with χ2 test.*

Tab.1

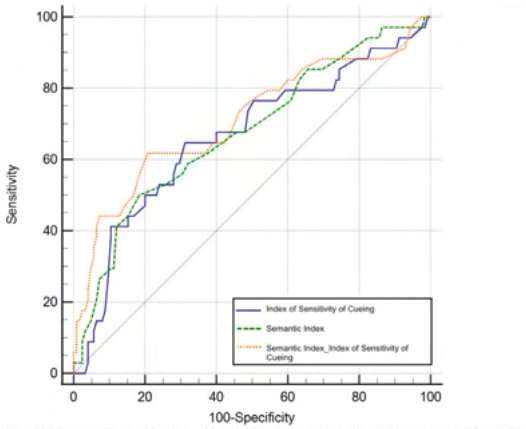

Figure 1. Comparison of ROC curves of Index of Sensitivity of Cueing (ISC), Semantic Index (SI) and the combination of SI and ISC.

Fig. 1

Table 2. Summary data from the ROC curves analysis with the values of Area Under the Curve (AUC) and the other dimensions related to the cut-off values selected, in all the three conditions (ISC, SI and SI+ISC).

	ISC	SI	SI+ISC
AUC	.664* (.554 - .774)	.676* (.597 - .748)	.710* (.600 - .820)
SENSITIVITY	.647	.500	.618
SPECIFICITY	.688	.816	.808
CUT-OFF VALUE	.548	.565	.279
YOUDEN'S INDEX	.335	.316	.426
ACCURACY	.679	.748	.767

** Comparisons between the three AUC are not significant using either De Long et al. (1988) and Hanley et al. (1982) methods.*

Tab. 2

Conclusion: AUC values of ISC and SI alone are low-moderate, and their combination does not improve their accuracy. These data suggest that alternative neuropsychological strategies possibly based on less used tests, such as theory of mind or decision-making tests, should be evaluated in association with the FCSRT to increase the accuracy of the differential diagnosis between AD and bvFTD.

Disclosure: Nothing to disclose.

EPR-204

Time perception dysfunction in stroke patients: a systematic review

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Background and aims: Time perception comprises the subjective experience of passing of time and of the duration of an event. We aim to describe time perception dysfunction in stroke patients.
Methods: We performed a systematic review of the literature in Pubmed, Medline, PsycInfo and Web of Science including manuscripts from their inception until December 2020. Keywords used were "time perception AND stroke" and "temporal processing AND stroke".
Results: A total of 25 manuscripts were selected, concerning a total of 396 patients (n=157 female, 39.6%). The majority of manuscripts (n=21) evaluated patients with ischaemic lesions. five manuscripts reported results from acute evaluations, while the majority referred to evaluations between two months and seven years after stroke. The majority of patients were submitted to brain MRI and right hemisphere lesions were present in 53% (n=211). Common reported lesion locations included the thalamus, insula, basal ganglia, dorsolateral prefrontal cortex, parietal cortex including supramarginal, angular gyrus and right inferior parietal cortex and cerebellum. Most studies (n=17) applied temporal evaluation protocols referring to prospective timing in sub- and supra-second task (2 seconds until 90 seconds), including visual and auditory stimuli time interval comparison, visual and auditory stimuli time estimation and time reproduction. Retrospective timing protocols involved mostly time duration estimation and evaluation of different temporal references. Under-estimation in temporal evaluation in sub- and supra-second was the most common dysfunction (n=10 studies).
Conclusion: There is still scarce knowledge about time perception deficits after stroke. A methodical search of this dysfunction in stroke patients is needed for further developments in this field.
Disclosure: Nothing to disclose.

Motor neurone diseases 1

EPR-205

Oro-facial and bulbar study in spinal muscular atrophy: a protocol feasibility

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Background and aims: Spinal Muscular Atrophy (SMA) is a genetic disorder caused by the deletion of the Survival Motor Neuron (SMN1) which leads to motor neuron death, resulting in loss of muscle strength. Motor neurons in the brainstem are affected as those in the spinal cord so that facial as well as muscles involved in bulbar functions are also impaired. The general aim of this project is to investigate strength and function of the oro-facial and brainstem muscles in patients with SMA over time, analyzing two main clinical domains: facial muscle strength and respiratory function.

Methods: This is a 2-year pilot and observational study involving patients with SMA of all types. To evaluate facial muscle strength patients underwent Iowa Oral Performance Instrument (IOPI) for lip and tongue strength, active Maximum Mouth Opening (aMMO) and Motor Unit Number Index (MUNIX) of orbicularis oculi. To evaluate respiratory function patients were assessed by diaphragm motility with ultrasound scan (Figure 1).

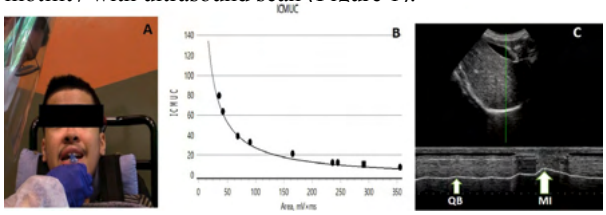

Figure 1. A Iowa Oral Performance Instrument (IOPI). B Motor Unit Number Index (MUNIX). C echo images of diaphragm (white line): to the left during quiet breath (QB), on the right at maximal inspiration (MI).

Results: We recruited 52 genetically confirmed SMA patients (27 males and 25 females): 8/52 with type 1 (16%), 22/52 with type 2 (42%) and 22/52 with type 3 (42%). At baseline evaluation 37/52 patients (71%) had already started treatment with nusinersen, instead 15/52 (29%) were naïve. All the evaluations were carried out in a standard of care setting. All the procedures well tolerated by patients, also by children.

Conclusion: The oro-facial and bulbar function should be a benchmark in the evaluation of the impact of novel therapies (such as nusinersen) in SMA patients.

Disclosure: Nothing to disclose.

EPR-206

Corneal Confocal Microscopy: Neurologic Disease Biomarker in Amyotrophic lateral sclerosis

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Background and aims: Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disorder primarily affects motor system with extra-motor involvement to a variable extent. Small-fiber neuropathy (SFN) has been identified in ALS by invasive skin biopsy. Corneal confocal microscopy (CCM) is a noninvasive technique to quantify small-fiber nerves and immune cells in the cornea. We used CCM as an imaging biomarker to evaluate SFN, and to monitor disease severity and progression in ALS.

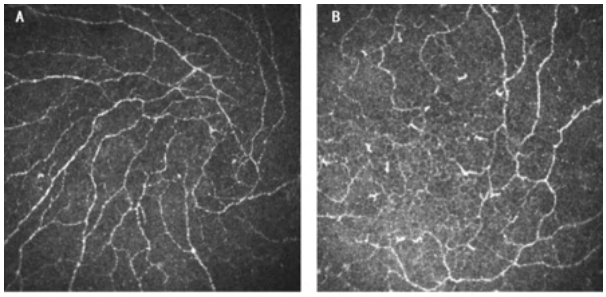
Methods: 66 ALS patients and 15 health controls underwent neurological evaluation and IVCM. For corneal nerve, IVCM images were analyzed both in the inferior whorl area (inferior whorl length (IWL)) and the peripheral area (including corneal nerve fiber length (CNFL), density (CNFD), branch density (CNBD)). For dendritiform cell, density was also calculated separately in the inferior whorl area (IWDC) and the peripheral area (CDC).

Results: IWL and CNFD were significantly lower while CNBD, IWDC and CDC were significantly higher in ALS compared to controls (table1). Within-case comparison showed significantly decreased IWL while increased IWDC in the inferior whorl area of late-phase patients compared to early-phase patients (17.51±3.44 vs 19.04±2.71, p=0.048; 55.51±55.02 vs 29.29±25.64, p=0.020; figure 1). Spearman analysis (figure 2) showed significant correlations between IWL and disease severity (p<0.001, r=0.457) as well as disease progression (p=0.002, r=-0.378).

		Control n=15	ALS n=66	*p* value
Corneal Nerve	**Inferior Whorl Area**			
	IWL (mm/mm²)	21.83(3.24)	18.33(3.14)	0.000
	Peripheral Area			
	CNFL (mm/mm²)	19.83(3.62)	17.80(3.79)	0.078
	CNFD (/mm²)	41.35(11.28)	33.90(7.64)	0.004
	CNBD (/mm²)	44.23(18.48)	58.40(22.70)	0.038
Dendritiform Cell Density	**Inferior Whorl Area**			
	IWDC (/mm²)	21.39(12.87)	41.60(43.76)	0.003
	Peripheral Area			
	CDC (/mm²)	7.69(8.52)	30.48(35.37)	0.000

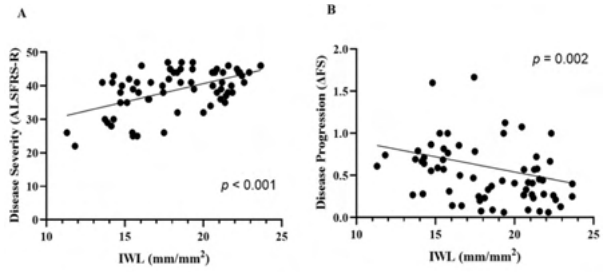
IWL, inferior whorl length; **CNFL**, corneal nerve fiber length; **CNFD**, corneal nerve fiber density; **CNBD**, corneal nerve branch density; **DC**, Dendritiform cells; **IWDC**, dendritiform cells in the inferior whorl area; **CDC**, dendritiform cells in the peripheral area

Table 1. Corneal confocal microscopy parameters in controls and ALS patients.



Disease phases was based on the King's College staging system (KCSS). Early-phase patients were in KCSS Stage 1 and 2. Late-phase patients were in KCSS Stage 3 and 4.

Figure 1. Corneal confocal microscopy images of the inferior whorl cornea in early-phase ALS patients (A) and late-phase ALS patients (B).



IWL, inferior whorl length; Disease severity was based on the Revised ALS Functional Rating Scale (**ALSFRS-R**); Disease progression was calculated by the declining rate of **ALSFRS-R** at assessment (**ΔFS**= (48-**ALSFRS-R** at assessment)/disease duration at assessment).

Figure 2. Correlation of inferior whorl length with disease severity and progression in ALS.

Conclusion: CCM is a noninvasive imaging biomarker to detect SFN in ALS. Quantification of corneal nerve and dendritiform cell in the inferior whorl area could well evaluate the severity and progression of ALS.
Disclosure: Nothing to disclose.

EPR-207

Epidemiology of ALS in Emilia Romagna Region, from 2009 to 2019: a prospective population-based study

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Background and aims: Our previous epidemiological study on ALS in Emilia Romagna Region of Italy showed a crude incidence rate of 2.63/100,000/year from 2009 to 2011, that was similar to figures reported for European countries based on existing population based registries. In this prospective population based study we describe demographic, clinical features and phenotypes of incident ALS cases in Emilia Romagna Region of Italy.
Methods: This is a prospective, population-based, epidemiological study conducted in a Region of Northern Italy (Emilia Romagna, 4.5 million inhabitants) where an ALS register is still collecting newly diagnosed ALS patients starting from 2009.
Results: From 1 January 2009 to 31 December 2019, 1,398 patients received a new diagnosis of ALS with a crude incidence rate of 2.86/100,000/year (male to female ratio: 1.33). The average age of onset was 67.69 (SD 11.35) years, with a higher age at onset for bulbar and respiratory phenotypes, and lower mean age at onset for carriers of C9orf72 mutation. The expected variation of ALS incidence with age was characterized, as already reported, by a progressive increase in incidence from the 40s leading to a peak at 70–75 years, followed by a sharp decrease. After this peak, in which the incidence was higher in men, there was a progressive increase in incidence in women.
Conclusion: Here we report incidence rates slightly higher than those reported by European registries, probably due to an older population characterizing our region. Our data confirm the already reported relationship among phenotype, sex, age, and gene mutation.
Disclosure: Nothing to disclose.

EPR-208

Whole and fractionated human platelet lysate induce neuroprotection in severe amyotrophic lateral sclerosis models

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Background and aims: Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease leading to a progressive, irreversible muscle paralysis and death 3–5 years after diagnosis. Our axis is the exploration of neurotrophic growth factors (NTFs) as a biotherapy and we developed a heated human platelet lysate (HPPL) which contain many growth factors and evaluated its therapeutic value in ALS.

Methods: We studied the protective properties of whole and fractionated (under 50/30/10 or 3kDa) HPPL against different cell death inducers in dopaminergic neurons and primary motor neuron culture. We evaluated the potency of HPPL and of 3kDa on SOD1G86R mice and compare it to the effect of riluzole (the only treatment available in ALS).

Results: Data in our two cell models showed the high protection potential of HPPL in many conditions (ferroptosis, apoptosis and global oxidative stress) whereas that of the fraction under 3kDa was more limited. Chronic delivery of HPPL by intra-cerebro-ventricular administration showed that the disease onset was delayed by seven days and the survival was increased by 48 days. When SOD1G86R mice were treated with intranasal administration of 3kDa fraction, no modification of the disease onset but a seven days extension of survival was observed. In the same conditions, riluzole treatment (per os) delayed the onset by 11 days with no changes in survival.

Conclusion: In conclusion we showed the benefits of using specific platelet lysate in ALS models. The results obtained by the fraction under 3kDa may highlight the role of platelet elements other than NTFs in neuroprotection.

Disclosure: Nothing to disclose.

EPR-209

Identifying "hidden" mutations unveil gene interactions that modify ALS phenotypes: Tunisian ALS cases

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Background and aims: Amyotrophic lateral sclerosis (ALS) is a devastating neurodegenerative disorder. The high genetic throughput methods had delineated more than 30 confirmed major and/or rare disease genes underlying ALS. However, the considerable dissimilarity in ALS phenotypes point to complex gene associations

Methods: Preliminary mutational screening for C9ORF72 was assessed before processing to NGS with custom 69 genes panel. Genetic study was conducted in instituto of Auxologico of Milan and the sequencing platform of faculty of Medicine of Tunis.

Results: The 1st case is fALS where the proband is carrying TARDBP-p.G294A and C9ORF72 expansion mutations. Although two cases shares C9ORF72 expansion, they developed different ALS form (spinal and bulbar).The proband had earlier age of onset (54 years vs.62), milder phenotype with slow progression unlike his sister (6 years vs.7 months) The 2nd case is sporadic ALS with TARDBP-p.G294A and C9ORF72 expansion mutations. He developed a spinal ALS in his fifties (52 years) and survived for five years. The 3rd bulbar fALS case is two ALS patients share TARDBP p.G294A mutation, but the proband was, additionally, mutated for SPG11-p.Trp1455Cys. The latter developed cognitive impairment and spasticity in inferior limb at 62 years.The disease duration was one year after diagnosis set with aggressive evolution. Interestingly, his cousin was diagnosed earlier at 55 years without atypical features.

Conclusion: We highlight the co-existence of two causative genes within the same ALS patient. Therefore, rather than limiting research on identifying one disease causing mutation, other genetic factors apart of the main gene needs to be determined.

Disclosure: Nothing to disclose.

EPR-210

G507D mutation in FUS gene causes familial amyotrophic lateral sclerosis with a specific genotype-phenotype correlation

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Background and aims: Mutations in the FUS gene have been described in patients with ALS being associated to a typical phenotype with young onset, aggressive course, high incidence of bulbar symptoms and early respiratory involvement. Among FUS mutations, p.G507D has been previously identified only in sporadic ALS cases. Here we firstly report a family carrying a missense mutation c.1520 G>A in FUS gene with a tight association with an atypical phenotype.
Methods: Family report: A 63-year-old man presented muscle weakness in the right leg followed with slow progression with selective posterior legs atrophy and atypical sparing of bulbar and respiratory district. A 55-year-old aunt presented a similar history of unilateral leg involvement, with a gradual spinal spreading. In his family tree, his father and uncle died for ALS after five years. Genetic analysis of FUS gene revealed a missense mutation c.1,520 G>A in a heterozygous pattern.
Results: Discussion: We described the first familial form of FUS-ALS due to G507D mutation with a phenotype characterised by LMN involvement at the lower limbs, slow progression, bulbar sparing and late respiratory failure, a clinical picture rarely described in FUS-ALS. Furthermore, we will discuss the genotype-phenotype correlation caught in our cases since a peculiar clinical feature represented by a disproportionate involvement in lower limbs muscles has been brought out.
Conclusion: Our report about segregation of FUS G507D mutation in ALS family strengthen its pathogenic role. Moreover, we establish a genotype-phenotype correlation between the above mentioned mutation and a peculiar phenotype, widening the clinical heterogeneity of FUS mutations.
Disclosure: I have no disclosure to declare

EPR-211

Impact of Nusinersen on Caregiver Experience and HRQoL in SMA Type II/III Participants: CS2/12-SHINE Study Results

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Background and aims: Participants with later-onset spinal muscular atrophy (SMA) treated with nusinersen in the Phase 1b/2a CS2 (NCT01703988) and CS12 study (NCT02052791) were eligible to enroll in SHINE (NCT02594124). The effects of nusinersen on caregiver experience and health-related quality of life (HRQoL) were evaluated among CS2/12-SHINE participants.
Methods: Interim data (27 August 2019) from SHINE were evaluated by SMA type. The mean (SD) age at screening in CS2 was 4.4 (4.0) and 8.9 (4.4) years in Type II and Type III participants, respectively. Assessment of Caregiver Experience with Neuromuscular Disease (ACEND) and Pediatric Quality of Life Inventory (PedsQL) Generic Core Scale and Neuromuscular Module were administered to caregivers of participants. ACEND and PedsQL scales are scored from 0–100 with higher scores indicating a reduced caregiver impact and improved HRQoL, respectively. The score changes from CS2 baseline to Day 1,290 in SHINE (~3.5 years of follow-up) were evaluated.
Results: There was an overall pattern of observed mean increases in ACEND scores among caregivers of participants with SMA Type III (n=14) from CS2 baseline to Day 1290 in SHINE across all seven subdomains (Table). A similar trend was found for caregivers of participants with SMA Type II (n=10) in all but one subdomain (Finance). PedsQL Generic Core Scale and Neuromuscular Module mean scores generally improved for participants with SMA Type II and III based on parent proxy reports.

Table. ACEND and PedsQL Parent Proxy Mean (95% CI) Change Scores from CS2 Baseline to Day 1290 in SHINE

	ACEND[a]	SMA Type II (n=10)	SMA Type III (n=14)
Physical Impact	Feeding/Grooming/Dressing	14.9 (8.60, 21.14)	4.9 (-2.99, 12.75)
	Sitting/Play	0.6 (-8.09, 9.29)	2.0 (-0.97, 4.97)
	Transfers	11.6 (-4.33, 27.43)	6.9 (1.15, 12.56)
	Mobility	15.3 (1.79, 28.78)	9.1 (0.91, 17.26)
General Caregiver Impact	Time	1.6 (-13.68, 16.81)	5.6 (-3.65, 14.81)
	Emotion	10.8 (-5.49, 27.02)	9.8 (2.93, 16.72)
	Finance	-6.8 (-16.80, 3.30)	3.2 (-4.80, 11.23)
	PedsQL Parent Proxy[a]	**SMA Type II (n=10)**	**SMA Type III (n=14)**
	Generic Core Scales	0.3 (-6.50, 7.13)	7.8 (-0.36, 15.86)
	Neuromuscular Module	2.5 (-4.89, 9.79)	5.6 (-0.63, 11.78)

[a]Positive changes indicate reduced caregiver impact on the ACEND and improvements in QoL on the PedsQL Parent Proxy

Table. ACEND and PedsQL Parent Proxy Mean (95% CI) Change Scores from CS2 Baseline to Day 1,290 in SHINE

Conclusion: Nusinersen was associated with reduced impact for caregivers and improvements in HRQoL for participants with later-onset SMA over 3.5 years as measured by the ACEND and PedsQL, respectively.
Disclosure: This study was sponsored by Biogen (Cambridge, MA, USA). Writing and editorial support for the preparation of this abstract was provided by Excel Scientific Solutions (Fairfield, CT): funding was provided by Biogen.

EPR-212

The collaboration between neurology and palliative care for people with ALS/MND in the UK

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Background and aims: People with ALS/MND have often received care for palliative care services – at home and in hospice inpatient units. The recent UK guidelines have recommended early involvement and that palliative care should be a regular member of the multidisciplinary team. This survey was to ascertain the extent of collaboration.
Methods: Details of an online survey were distributed by the Association of Palliative Medicine, which represents doctors working in palliative care.
Results: 86 specialists responded – representing about 40% of specialist palliative care units in the UK. 97% saw ALS/MND patients. Their multidisciplinary teams (MDT) rarely involved speech and language therapy (20%) or dietitians (32%). The time when they would accept referral varied but the majority were involved early in the disease progression. 86% collaborated with neurology services, with 60% being part of the MDT and 53% having regular telephone contacts. Neurologists were rarely a barrier to referral (16%) and patient or family reluctance to see palliative care was rare (13%). 41% were planning further collaboration and 95% felt that collaboration was helpful in-patient care.
Conclusion: The majority of the respondents were involved in ALS/MND care and many were part of wider MDTs. Specialist palliative care may have restricted access to speech and language therapy and dietary advice, which may disadvantage patients with ALS/ MND. Overall, there is good collaboration and this is seen to be helpful. However, the respondents may be those most involved in ALS/MND care and may not be representative of the whole of the UK.
Disclosure: No disclosures. to be made

EPR-213

The care of people with ALS – the collaboration between neurology with palliative care across Europe

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Background and aims: Palliative care services are often involved in the care of people with ALS. This study asked palliative care specialists across Europe how they collaborated with neurology in providing care for ALS patients.
Methods: A voluntary online survey was advertised through palliative care and neurology associations for completion by palliative care specialists. The survey assessed details of their services and their involvement with ALS.
Results: Of the 298 people starting the survey, 126 completed, from 11 European countries, with the majority from Switzerland (13%) and Italy (74%). Overall, most worked in community (75%) or inpatient settings (79%). Their teams were multidisciplinary but occupational therapy (27%), speech and language therapy (22%) and spiritual care (41%) were less represented. 94% reported seeing people with ALS, with 40% only becoming involved when patients were at the end of life or the terminal phase. There was evidence of joint working with neurology, the commonest being joint clinics (33%) and regular telephone contact (44%). Barriers to collaboration included the reluctance of neurology to refer (42%), financial or resource issues (20%) and patient or family reluctance to see palliative care (17%). Further analysis will be presented comparing responses from Switzerland and Italy.
Conclusion: Palliative care services are involved in the care of people with ALS but often only in the later stages of disease progression, despite guidelines recommending earlier involvement. There is the need for continued education of both neurology and palliative care services in the role of palliative care for neurological patients.
Disclosure: There are no disclosures.

Movement disorders 4

EPR-214

Is directional stimulation superior to omnidirectional stimulation in reducing the dose of antiparkinsonian medications?

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Background and aims: The technique of deep brain stimulation (DBS) has undergone a remarkable improvement. The development of directional electrodes is one of the most important milestones in this technical evolution. Although continuously evolving data supports the fact that directional subthalamic DBS has a wider therapeutic window, lower therapeutic current strength, and better normalized therapeutic window percentage, no comparative studies have been conducted on the level of postoperative reduction in the daily dose of oral antiparkinsonian medications after directional versus omnidirectional DBS.
Methods: A single-center, prospective trial was performed to compare the reduction in the daily administered dose of antiparkinsonian medications following directional versus omnidirectional bilateral subthalamic DBS in advanced Parkinson's disease.
Results: A total of 37 patients with directional DBS and 37 subjects with omnidirectional DBS were enrolled. Demographic-, disease- and medication-related characteristics at baseline (preoperative examinations) were identical between the two groups. Demographic, disease-, and medication-related data were reassessed, and all patients underwent detailed neurological and neuropsychological examinations one day, six months and 12 months postoperatively. Differences in the change in levodopa equivalent daily dose, the number of patients receiving oral monotherapy and not treated with levodopa after the surgery, and the number of postoperative tablets of the required daily antiparkinsonian medications were compared between the two groups.
Conclusion: Assuming that directional stimulation is more efficient than omnidirectional stimulation, it can be hypothesized that directional stimulation may lead to greater reduction in the total daily administered dose of antiparkinsonian medications. Our findings can be important for future cost-effectiveness calculations.
Disclosure: This study was supported by the ÚNKP-20-4 New National Excellence Program of the Ministry for Innovation and Technology from the Source of the National Research, Development and Innovation Fund and a grant from Abbott Laboratories.

EPR-215

Connection between olfactory dysfunction and severity of tremor: new hypothesis

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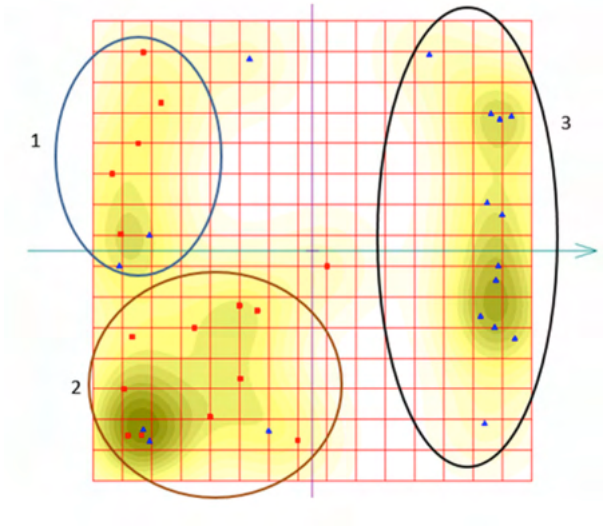
Background and aims: Parkinson's disease (PD) and essential tremor (ET) are among the leading neurological diseases worldwide. Varying in manifestation, it exhibits some differences: rest tremor for PD and postural-kinetic for ET. Olfactory dysfunction is the first manifest of PD often preceding the movement disorders. Our aim was to obtain tremor data of PD and ET patients and the results of their olfactory function, which can help verify our scientific hypothesis on the inverse relation between tremor manifestation and olfactory dysfunction: lower tremor is accompanied with worse smell perception, and vice versa.
Methods: We had three groups of patients: suffering from PD, ET and healthy people. An examination procedure of olfactory function was based on extended olfactory Sniffin' sticks test with three parameters: threshold, identification and discrimination. For tremor testing we used wireless device to monitor electrophysiological signals with three main characteristics: skin electromyogram (SEMG), gyroscope and accelerations. We used an elastic map technique to cluster and analyze all data.

Wireless device for study tremor

Sniffin' sticks test

Results: Proven inverse relation between tremor level and olfactory dysfunction is the core result of our work. Indeed, ET patients showed better olfactory function results accompanied by stronger tremor, as compared to PD patients: lower tremor with worse smell perception.



Clustering of PD patients (red sqaures) vs. ET patients (blue triangles)

Conclusion: Combination of olfactory testing and tremor records improves significantly the discrimination of PD patients from those with ET, as well from healthy people. The presented results could be implemented for early differential diagnostics of PD vs. ET, as well as for the improvement of individual therapy course for such patients.
Disclosure: Nothing to disclose.

EPR-216

Meta-Analysis and Systematic Review of Galvanic Vestibular Stimulation on Postural Control in Parkinson's disease

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Background and aims: Subthreshold Galvanic Vestibular Stimulation (GVS) may improve postural control in Parkinson's disease (PD) patients. This systematic review and meta-analysis investigate the effects of GVS on motor and non-motor outcomes in PD patients.
Methods: Six separate databases as well as ongoing trial and research registers were searched for randomised, controlled trials with a parallel or cross-over design that evaluated the effects of GVS on gait and balance in PD. Inclusion criteria were outcome measures of functional mobility, subjective balance, motor tasks, reactive balance and static balance. We excluded non-peer reviewed literature, conference proceedings and studies where it was not possible to extract results due to missing information. We used standardized mean difference (Hedges' g) as a measure of effect size in all studies.
Results: A total of 223 studies were screened and 14 included of which six qualified for the meta-analysis. A random effects model meta-analysis found GVS to be more effective than sham GVS for the improvement in postural outcome measures. The overall effect size was 1.28 (95% CI 1.02–1.61) and had low heterogeneity (Q=20.05, df=11, p=0.04, I^2=33.2%). However, the random effects model found no significant effect of GVS within each subgroup. A trim and fill funnel plot showed publication bias to be unlikely.
Conclusion: GVS may enhance gait and balance in patients with Parkinson's disease, but better powered studies that assess clinically useful outcome measures are required.
Disclosure: Nothing to disclose.

EPR-217

Selected genetic polymorphisms of COMT, DRD2, ANKK1, and DAT genes and the risk of psychosis in Parkinson's disease

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Background and aims: Recent studies explored polymorphisms of multiple genes as possible genetic substrate of psychosis in Parkinson's disease (PPD). This study aimed to examine the association of seven selected polymorphisms of DRD2, ANKK1, COMT and DAT genes with PPD onset.
Methods: The study included 234 PD patients who underwent neurological examination, assessment of depression and anxiety and cognitive screening. Genotyping of rs4680 in COMT, rs2283265, rs1076560, and rs6277 in DRD2, rs1800497 and rs2734849 in ANKK1 genes was performed using TaqMan SNP genotyping assays (ThermoFisher Scientific, Foster City, CA) on the ABI Prism 7500 Fast Real-Time PCR System (Applied Biosystems, USA). PCR and subsequent agarose gel electrophoresis were used to detect variable number of tandem repeats (VNTR) polymorphism in the DAT gene.
Results: Out of 234 PD patients, 101 (43.2%) patients had PPD. We found higher risk of developing psychosis 2.3 times in AA rs6277 DRD2 carriers and 2.2 times higher risk in GG rs2734849 ANKK1 carriers (p=0.027, and p=0.031 respectively). Multivariate regression analysis demonstrated that independent predictors of the onset of psychosis in group of PD patients were: LEDD 900mg (OR=2.041, 95%CI: 1.089–3.824, p=0.026), UPDRS III part score (OR=1.025, 95%CI: 1.001–1.050, p=0.044), HDRS total score 7 (OR=2.846, 95%CI: 1.289–-6.286, p=0.010), HARS total score >14 (OR=2.236, 95%CI: 1.061–4.710, p=0.034) and GG homozygotes of rs2734849 ANKK1 gene (OR=2.588, 95%CI: 1.325–5.054, p=0.005).
Conclusion: We found that rs6277 of DRD2 gene and rs2734848 of ANKK1 gene are associated with PPD. Genotypes AA rs6277 DRD2 and GG rs2734849 ANKK1 double the risk of PPD development.
Disclosure: Nothing to disclosure

EPR-218

Effectiveness of Opicapone in Parkinson's according to baseline use of MAO-B inhibitors & DA: real-world OPTIPARK study

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Background and aims: Opicapone (OPC) proved to be effective in treating end-of-dose motor fluctuations (MF) in Parkinson's disease (PD) patients [1,2]. The OPTIPARK study evaluated OPC 50mg in a heterogeneous population of patients treated in real-world conditions [3].
Methods: OPTIPARK was a prospective, open-label, single-arm trial conducted in Germany and the UK. Patients with MF received OPC 50mg in addition to current antiparkinsonian treatment. Primary efficacy 3-month endpoint was Clinician's-Global-Impression-of-Change (CGI-C). Secondary efficacy endpoints included Patient's-CGI-C (PGI-C), 8-item PD-Questionnaire (PDQ-8), Unified PD Rating Scale (UPDRS) and Non-Motor Symptoms Scale (NMSS). Safety assessments included evaluation of treatment-emergent adverse events (TEAEs). This post-hoc analysis evaluated, for each outcome, the influence according to baseline use of both monoamine-oxidase-B inhibitors (MAO-Bi) and dopamine agonists (DA) in patients who completed the study.
Results: 393 (82.4%) patients completed the 3-month endpoint (completers-set, Table 1). Of these, patients using MAO-Bi/DA at baseline experienced greater improvements on CGI-C and PGI-C, when compared to patients NOT using MAO-Bi/DA at baseline (Table 2). Except for NMSS, patients NOT using MAO-Bi/DA at baseline experienced greater improvements on UPDRS-II and III and quality-of-life (PDQ-8) (Table 3). Lower incidence of TEAEs considered at least possibly related to OPC were also reported for patients using MAO-Bi/DA at baseline (Table 3).

Table 1. Baseline characteristics (Completer-Set)

Category	Used MAO-Bi & DA at Baseline N=145	Not Used MAO-Bi & DA at Baseline N=248
Age, mean (SD)	64.6 (9.1)	68.6 (8.8)
Male, n (%)	92 (63.4)	165 (66.5)
PD duration, mean (SD) years	8.8 (4.4)	8.2 (4.8)
Onset of MF, mean (SD) years	2.3 (2.8)	2.5 (3.1)
Ldopa amount, mean (SD) mg	487 (220)	600 (253)

SD, standard deviation; PD, Parkinson's Disease; MF, motor fluctuations; OMF, onset of MF

Table 2. CGI-C and PGI-C results after 3 months (Completer-Set)

Category	Used MAO-Bi & DA at Baseline N=145 n (%)	Not Used MAO-Bi & DA at Baseline N=248 n (%)
CGI-C		
Not assessed	-	-
Very much improved	11 (7.6)	19 (7.7)
Much improved	67 (46.2)	100 (40.3)
Minimally improved	38 (26.2)	85 (34.3)
No change	20 (13.8)	36 (14.5)
Minimally worse	6 (4.1)	7 (2.8)
Much worse	2 (1.4)	1 (0.4)
Very much worse	1 (0.7)	-
PGI-C		
Not assessed	-	-
Very much improved	6 (4.1)	24 (9.7)
Much improved	73 (50.3)	86 (34.7)
Minimally improved	31 (21.4)	82 (33.1)
No change	19 (13.1)	39 (15.7)
Minimally worse	13 (9.0)	12 (4.8)
Much worse	2 (1.4)	4 (1.6)
Very much worse	1 (0.7)	1 (0.4)

OMF, onset of motor fluctuations; CGI-C, Clinician's Global Impression of Change; PGI-C, Patient's Global Impression of Change

Table 3. Secondary, after 3 months, and safety outcomes (Completer-Set)

Category	Used MAO-Bi & DA at Baseline N=145	Not Used MAO-Bi & DA at Baseline N=248
UPDRS II (at ON stage), mean (SD)	-1.5 (3.6)	-1.7 (3.8)
p-value	*<.0001*	*<.0001*
UPDRS III, mean (SD)	-4.3 (7.9)	-4.8 (8.2)
p-value	*<.0001*	*<.0001*
PDQ-8, mean (SD)	-2.8 (11.1)	-3.8 (13.7)
p-value	*0.0034*	*<.0001*
NMSS, mean (SD)	-7.7 (19.6)	-6.3 (19.8)
p-value	*<.0001*	*<.0001*
Any TEAE, n (%)	100 (69.0)	181 (73.0)
At least possibly related[a] TEAEs, n (%)	52 (35.9)	102 (41.1)

OMF, onset of motor fluctuations; SD, standard deviation; UPDRS, Unified Parkinson's Disease Rating Scale; PDQ-8, 8-item Parkinson's Disease Questionnaire; NMSS, Non-Motor Symptoms Scale; p-values obtained through Student's t-test for the change from baseline; [a]relationship to study medication reported as 'possible', 'probable', 'definite' or missing; TEAE, treatment-emergent adverse event (with onset or worsening after first opicapone intake until study termination, either regularly or prematurely)

Conclusion: Overall, these findings indicate that patients may similarly benefit using or not MAO-Bi/DA and OPC 50 mg as adjunctive therapy to levodopa.

Disclosure: 1.Ferreira et al., Lancet Neurology 2016;15 (2):154-165; 2.Lees et al., JAMA Neurol. 2017;(2):197–206; 3.Reichmann et al., Transl Neurodegener. 2020;9(1):9

EPR-219

Opicapone in Parkinson's patients with motor fluctuations and complications of therapy at baseline: the OPTIPARK study

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Background and aims: Opicapone proved to be effective in treating end-of-dose motor fluctuations in Parkinson's disease (PD) patients [1,2]. The OPTIPARK study evaluated opicapone 50-mg in a heterogeneous population of patients treated in real-world conditions [3].

Methods: OPTIPARK was a prospective, open-label, single-arm trial conducted in Germany and the UK. Patients with motor fluctuations received opicapone 50mg in addition to current antiparkinsonian treatment. Primary efficacy 3-month endpoint was Clinician's-Global-Impression-of-Change. Secondary assessments included Unified-Parkinson's-Disease-Rating-Scale (UPDRS) and treatment-emergent adverse events (TEAEs). This post-hoc analysis evaluated the impact of OPC in patients who completed the study and reported complications of therapy (CoT) at baseline, assessed by UPDRS IV.A-32 (waking-day-dyskinesias, WdD).

Results: 393 (82.4%) patients completed the 3-month endpoint (completers-set) and 150 reported WdD at baseline (Table 1). Most baseline WdD were not- or mildly-disabling and also not- or slightly-painful. Approximately 26% of these WdD completers reported dyskinesia as TEAE during the study. At endpoint, most (131, 88%) of patients either maintained (54%) or improved (34%) WdD. Most remaining WdD were still not- or mildly-disabling and also not- or slightly-painful (Table 2, Figure 1). Notably, none worsened to either severe- or complete-disabling and severe- or marked-painful. Approximately 54% of dyskinesia reported as TEAE resolved following a mean daily levodopa decrease of ~67mg (Table 2).

Table 1. Demographics and other baseline characteristics (completers set)

Characteristic	Baseline (N=393)	
Male gender, n (%)	257 (65.4)	
Age, mean (SD) years	67.2 (9.1)	
L-dopa amount (mg), mean (SD)	557.8 (247)	
Disease duration, mean (SD) years	8.4 (4.6)	
Duration of motor fluctuations, mean (SD) years	2.4 (3.0)	
UPDRS IV. Complications of Therapy		
A. Dyskinesias		
32. What proportion of the waking day are dyskinesias present?	**Baseline (N=393)**	
None, n (%)	243 (61.8)	
L-dopa amount (mg), mean (SD)	*533.0 (248)*	
1-25% of day, n (%)	97 (24.7)	N=150
26-50% of day, n (%)	38 (9.7)	
51-75% of day, n (%)	10 (2.5)	*L-dopa (mg), mean (SD)*
76-100% of day, n (%)	5 (1.3)	*598.0 (241)*

SD, standard deviation

Table 2. Follow-up of Patients that at baseline reported dyskinesia during waking day

	Baseline (N=149*)	During the Study *Imp.*	*Maint.*	*Wors.*	Endpoint
UPDRS IV. Complications of Therapy					
A. Dyskinesias					
32. What proportion of the waking day are dyskinesias present?					
None, n (%)	-	-	-	-	24 (16.1)
1-25% of day, n (%)*	96 (64.4)	*18 (12.1)*	*66 (44.3)*	*12 (8.1)*	89 (59.7)
26-50% of day, n (%)	38 (25.5)	*23 (15.4)*	*10 (6.7)*	*5 (3.4)*	22 (14.8)
51-75% of day, n (%)	10 (6.7)	*7 (4.7)*	*2 (1.3)*	*1 (0.7)*	8 (5.4)
76-100% of day, n (%)	5 (3.4)	*3 (2.0)*	*2 (1.3)*	*0*	6 (4.0)
33. How disabling are the dyskinesias?					
Not disabling, n (%)	64 (43.0)	-	*54 (36.2)*	*10 (6.7)*	80 (53.7)
Mildly disabling, n (%)	44 (29.5)	*15 (10.1)*	*23 (15.4)*	*6 (4.0)*	50 (33.6)
Moderately disabling, n (%)	34 (22.8)	*26 (17.4)*	*8 (5.4)*	*0*	18 (12.1)
Severely disabling, n (%)	7 (4.7)	*6 (4.0)*	*1 (0.7)*	*0*	1 (0.7)
Completely disabled, n (%)	-	-	-	-	-
34. How painful are the dyskinesias?					
No painful dyskinesias, n (%)	111 (74.5)	-	*101 (67.8)*	*10 (6.7)*	117 (78.5)
Slight, n (%)	21 (14.1)	*11 (7.4)*	*8 (5.4)*	*2 (1.3)*	21 (14.1)
Moderate, n (%)	15 (10.1)	*10 (6.7)*	*5 (3.4)*	*0*	10 (6.7)
Severe, n (%)	1 (0.7)	*0*	*1 (0.7)*	*0*	1 (0.7)
Marked, n (%)	1 (0.7)	*1 (0.7)*	*0*	*0*	-
Reported Dyskinesias as TEAE	**Baseline**	**During the Study**			**Endpoint**
Any dyskinesia, n (%)	-	**39 (26.2)**			**18 (12.1)**
L-dopa amount (mg), mean (SD)	*644.9 (237)*	-			*577.6 (272)*
Mild	-	31 (79.5)			14 (77.8)
Moderate	-	9[$] (23.1)			4 (22.2)
Related[#]	-	32 (82.1)			13 (72.2)
Unlikely/unrelated	-	8[$$] (20.5)			5 (27.8)

* one subject had missing data at endpoint; Imp., improved; Maint., maintained; Wors., worsened; TEAE, treatment emergent adverse event; # Related TEAEs are defined as being at least possible related; $ one subject reported both mild and moderate; $$ one subject reported both unlikely and probable

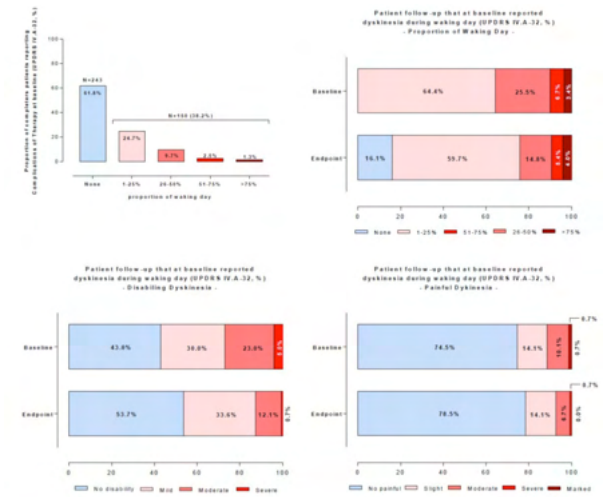

Figure 1. Follow-up of Patients that at baseline reported dyskinesia during waking day

Conclusion: In clinical practice, opicapone was not associated with a clear WdD worsening in patients already reporting CoT; in fact, more than double patients reported improvement rather than worsening.

Disclosure: 1.Ferreira et al., Lancet Neurology 2016;15 (2):154-165; 2.Lees et al., JAMA Neurol. 2017;74(2):197–206; 3.Reichmann et al., Transl Neurodegener. 2020;9(1):9

EPR-220

Opicapone in Parkinson's German Patients with Motor Fluctuations: findings from the OPTIPARK Study

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Background and aims: Opicapone (OPC) proved to be effective in treating end-of-dose motor fluctuations in Parkinson's disease (PD) patients [1,2]. The OPTIPARK study evaluated OPC 50-mg in a heterogeneous population of patients treated in real-world conditions [3].

Methods: OPTIPARK was a prospective, open-label, single-arm, multicentre trial conducted in Germany and the UK. Patients with motor fluctuations received OPC 50-mg in addition to current antiparkinsonian treatment. Primary efficacy endpoint was Clinician's Global Impression of Change (CGI-C) after three months. Secondary efficacy endpoints included Patient's GI-C (PGI-C) and Unified Parkinson's disease Rating Scale (UPDRS). Safety assessments included evaluation of treatment-emergent adverse events (TEAEs). Here Germany-only data is reported.

Results: 363 patients took one OPC dose (Safety Set; Table 1) and 291 completed three months' treatment. Of 349 patients with post-baseline efficacy data (Full Analysis Set), 70.8% and 76.3% experienced any (very much/much/minimal) improvement on CGI-C and PGI-C after three months, respectively (Table 2). There were relevant improvements on UPDRS II and III scores (Table 3). TEAEs considered at least possibly related to OPC were reported for 37.7% of patients, the most frequently reported being dyskinesia (5.8%) and dry mouth (4.4%). 91.7% of TEAEs were of mild or moderate intensity. Serious TEAEs considered at least possibly related to OPC were reported for five (1.4%) patients.

Table 1. Baseline characteristics (Safety Set)

Characteristic	N=363
Male gender, n (%)	234 (64.5)
Age, mean (SD) years	67.8 (9.2)
Disease duration, mean (SD) years	8.4 (4.9)
Duration of motor fluctuations, mean (SD) years	2.5 (3.3)

SD, standard deviation

Table 2. CGI-C and PGI-C results after 3 months (Full Analysis Set)

Category	CGI-C N=349	PGI-C N=291
Not assessed	2 (0.6)	0
Very much improved	16 (4.6)	16 (5.5)
Much improved	127 (36.4)	120 (41.2)
Minimally improved	104 (29.8)	86 (29.6)
No change	66 (18.9)	49 (16.8)
Minimally worse	23 (6.6)	15 (5.2)
Much worse	10 (2.9)	15(1.7)
Very much worse	1 (0.3)	0

CGI-C, Clinician's Global Impression of Change; LOCF, Last Observation Carried Forward; PGI-C, Patient's Global Impression of Change; LOCF applied to CGIC

Table 3. Changes from baseline in UPDRS scores (Full Analysis Set)

Scale	N	Mean (SD) change from baseline to 3 months	p-value
UPDRS II (activities of daily living) score at OFF stage	288	-3.3 (4.5)	<0.0001
UPDRS II (activities of daily living) score plus III (motor function) score at ON stage	291	-7.3 (10.1)	<0.0001
UPDRS III (motor function) score at ON stage	291	-5.3 (7.9)	<0.0001

SD, standard deviation; UPDRS, Unified Parkinson's Disease Rating Scale; p-values obtained through Student's t-test

Conclusion: OPC 50-mg was effective and generally well tolerated in German PD patients with motor fluctuations treated in clinical practice.

Disclosure: 1.Ferreira et al., Lancet Neurology 2016;15 (2):154-165; 2.Lees et al., JAMA Neurol. 2017;74(2):197–206; 3.Reichmann et al., Transl Neurodegener. 2020;9(1):9

EPR-221

PREDISTIM: a French multi-modal cohort to predict STN DBS response in PD on quality of life and refine its indication.

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Background and aims: Early occurrence of dementia and severe axial disorders after the subthalamic nucleus (STN) deep brain stimulation (DBS) may impede its benefit. Determine predictive factors of quality of life, one and five years after STN-DBS to refine DBS indication with multimodal parameters is pivotal for parkinsonian patients (PD).

Methods: 17 French expert centers from the NS-Park network have implemented a web-based solution to prospectively collect clinical information from PD patients' candidates to DBS. Protocol include three visits: inclusion, 1y and 5y post-surgery. Clinical data include demography, risk factors, motor/non-motors symptoms, adverse event, stimulation parameters, treatments. In parallel, biological samples/MRIs were performed to create a biobank/brain-imaging bank.

Results: PREDISTIM cohort includes 647 advanced PD patients. Motor/non-motor data are collected into an eCRF. A central biobank ensures quality/conformity of all biological samples (DNA/plasma/serum/CSF). A central brain-imaging bank ensure the quality of all MRIs sequences. Statistical approaches with joint latent class analysis, linear mix model analysis and machine learning will be used.

Conclusion: PREDISTIM is the largest prospective multi-centric cohort of PD patients at the stage of severe motor fluctuations. It will allow 1) to define weighted/multimodal predictors of STN DBS response on quality of life at five years 2) to refine new DBS inclusion criteria with a decisional tree including new parameters and 3) to assess surrogate biomarkers of disease progression from advanced stage to late stage with dementia and severe axial disorders in order to stratify PD population for future trials on advanced disorders contributing to the precise medicine.

Disclosure: No conflict of interest.

EPR-222

Postural instability in DYT-TOR1A dynamically dependent on sensory state

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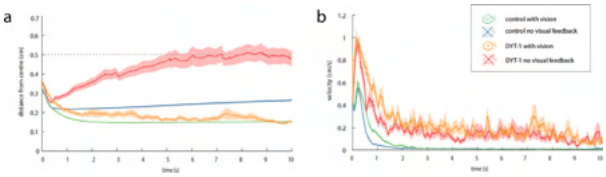
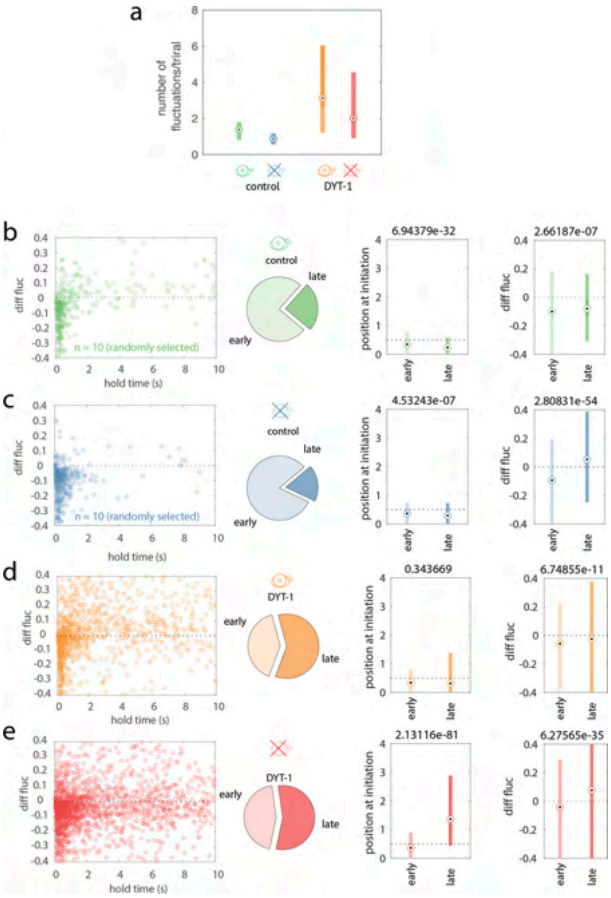
Background and aims: Dystonia is clinically defined as a disorder of posture yet there has been little systematic exploration of postural control in the laboratory.

Methods: Patients with DYT-TOR1A dystonia held the handle of a planar robotic arm to make point-to-point reaching movements with their symptomatic right arm. Reaches were made from a central start box to eccentric targets (15°, 135°, 225° or 315°). Position was then held within the target box for 10s. Estimation of arm position was dependent on proprioceptive and visual feedback (experimentally manipulated with balanced pseudo-randomization: cursor visible or not visible).

Results: During the hold phase, in the dystonia group, mean velocity did not resolve to zero in either feedback condition with increased fluctuations (movements associated with a velocity peak) consistently interrupting postural stability. By the end of the hold phase, in the dystonia group, a performance segregation across feedback conditions occurred; with visual feedback (high accuracy, low variability, in line with controls); with no visual feedback (low accuracy, high variability, significant deficit).



Group performance during hold a | mean radial distance from the center of the target (y-axis, cm) and b | mean velocity (y-axis, cm/s) over 10 second hold phase (x-axis, s) are shown with shaded standard error.



Fluctuations a | Total number of fluctuations per trial by subgroup b | green = controls with vision c | blue = controls with no visual feedback d| orange = DYT-1 with vision e | red = DYT-1 with no visual feedback.

Conclusion: To gain insight into mechanism we defined the motor control of holding within a Partially Observable Markov Decision Process. By manipulating noise parameters for sensory feedback and central motor stability we were able to reproduce the empirical data and discuss whether dystonia is a disorder of central motor instability or dysfunctional sensory processing. By using DYT-TOR1A as a prototype for dystonia, our results refine aetiological models, assist the design of biomarkers and inform rehabilitation strategies.

Disclosure: Nothing to disclose.

MS and related disorders 4

EPR-223

Retinal dysfunction in acute optic neuritis: inflammation at the inner nuclear layer or retrograde axonal signaling?

L. Del Porto [1], I. Kleerekooper [1], A. Petzold [2], A. Trip [3], G. Plant [3], L. Del Arti [3], J. Guajardo [3], S. Leo [3], A. Robson [3], G. Holder [3]

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Background and aims: Inner nuclear layer (INL) thickening is associated with poor visual recovery in optic neuritis (ON) and inflammatory activity in multiple sclerosis (MS). This study explores the structure-functional correlates of retinal dysfunction in acute ON to elucidate the underlying mechanisms.

Methods: A cross-sectional study of acute ON patients (<14 days). Subjects underwent pattern electroretinography (PERG), pattern visual evoked potentials (PVEP), visual acuity testing and optical coherence tomography imaging.

Results: 26 patients with acute ON (11 with MS, six myelin oligodendrocyte glycoprotein associated ON [MOGON], nine idiopathic ON) were recruited and compared to control data. PERG P50 and N95 amplitudes were significantly reduced in ON affected eyes (median 2.3V; range 0.8–5.0V and 3.4V; range 1.2–5.1V, respectively) compared with control data (4.0V; range 2.6–4.6V and 5.6V; range 4.6–6.8V; $p=0.003$ and $p<0.001$, respectively), and in ON affected compared with fellow eyes (both $p<0.001$). P50 peak times were significantly shortened in ON ($p<0.001$). P50 was positively correlated to INL thickness ($rs=0.36$; $p=0.009$) and there was a positive correlation between ganglion cell and inner plexiform layer (GCIPL) thickness and both P50 and N95 amplitudes ($rs=0.44$, $p=0.022$ and $rs=0.46$, $p=0.002$, respectively).

Conclusion: The structure-function interaction which localizes to the GCIPL and INL and the reduction in PERG P50 amplitude confirm that the early inflammatory processes in ON involves the macula. This could be due, separately or in combination, to: opening of the blood-retina barrier; activation of glia; or acute retrograde effects of optic nerve damage, likely to be metabolic.

Disclosure: AP reports that the Amsterdam UMC (location VUmc) MS Centre Amsteram and neuro-ophthalmology Expert Centre participated in the OCTIMS trial and the centre has received research support for OCT projects from the Dutch MS Society.

EPR-224

Effectiveness and Tolerability of Ofatumumab Versus First-line DMTs in Early RMS Patients: Phase 3b STHENOS Study Design

X. Montalban [9], R. Linker [1], D. Centonze [2], B. Turner [3], R. Sanchez-de la Rosa [4], L. Nillos [5], B. Ettle [6], E. Raponi [7], E. Thouvenot [8]

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Background and aims: Ofatumumab is a fully human anti-CD20 monoclonal antibody developed for the treatment of relapsing forms of multiple sclerosis (RMS) using a subcutaneous monthly 20 mg regimen. Here we present the design of the Phase 3b STHENOS study. This study will explore efficacy, safety, tolerability and Patient Reported Outcomes (PROs) of ofatumumab versus first-line, self-administered disease-modifying treatments (DMTs) of physician's patient's choice (Standard-of-Care [SoC]) in early RMS patients.

Methods: STHENOS is a prospective, open-label, rater-blinded, multicentre, parallel-arm, active comparator study in early RMS patients (aged 18–45 years; Expanded Disability Status Scale score 0–3, defined as newly-diagnosed patients or have never been on active treatment at study entry with three years from first MS symptoms). Patients will be randomised (1:1) to ofatumumab or SoC DMT (glatiramer acetate, interferons, teriflunomide, or dimethyl fumarate). The study consists of screening (60 days) and treatment (15 months)
periods, with a safety extension (6months) for patients withdrawing from ofatumumab. The primary endpoint is No Evidence of Disease Activity (NEDA-3) defined as absence of relapses, new MRI activity, and 3-month confirmed disability worsening at Month 15. Key secondary and exploratory endpoints are listed in Table-1.

Primary endpoint	NEDA-3 status (yes or no) at Month 15, defined as absence of confirmed clinical relapse, absence of new MRI activity (Gd+ T1 lesion or new/enlarged T2 lesion) with MRI re-baselined at Month 3 and absence of 3-month confirmed disability worsening
Secondary endpoints	1. Annual Relapse Rate 2. Time to first relapse 3. Proportion of relapse-free patients at Month 3, 9 and 15 4. Proportion of relapse-free patients with MRI activity-free (no new Gd+ T1 lesion or new/enlarged T2 lesion) at Month 3, 9 and 15 5. Time to 3-month/ 6-month Confirmed Disability Worsening 6. Change in EDSS from baseline to end of study 7. Number and volume of Gd+ T1 lesions 8. Number and volume of new/enlarging T2 lesions of brain
Exploratory endpoints	1. Safety and tolerability (AEs, SAEs, treatment discontinuations) 2. Compliance to treatment using patient diary 3. Cognitive Processing Speed (SDMT) 4. Serum biomarkers a. Neurofilament light chain b. Glial Fibrillary Acidic Protein 5. Patient Reported Outcomes a. Change in MSIS-29 (QoL) b. Change in FSIQ-RMS (Fatigue) c. Change in TSMQ-1.4 (Patient- satisfaction) d. Change in MSTCQ (Patient- injection experience) e. Change in MHI-5 (Mental health) f. Work productivity direct questions g. Social life and activities impact direct questions

AE, adverse event; EDSS, Expanded Disability Status Scale; FSIQ, Fatigue symptoms and impacts questionnaire; Gd+, gadolinium-enhancing; MHI, Mental health inventory; MRI, magnetic resonance imaging; MSIS, Multiple Sclerosis Impact Scale; MSTCQ, Multiple sclerosis treatment concerns questionnaire; NEDA, No evidence of disease activity; QoL, quality of life; RMS, relapsing multiple sclerosis; SAE, serious AE; SDMT, Symbol Digit Modalities Test; TSMQ, Treatment satisfaction questionnaire for medication

Table 1. Phase 3b STHENOS study endpoints

Results: STHENOS plans to enroll ~236 RMS patients from ~50 sites across France, Italy, Spain, United Kingdom and Germany. The first-patient-first-visit is scheduled for March 2021 and final results are expected by September-2023.

Conclusion: STHENOS will provide clinical data and patient reported outcomes for an early RMS population treated with ofatumumab in a real-world scenario. This study will also complement the existing Phase 3 programme of ofatumumab.

Disclosure: This study was funded by Novartis Pharma AG, Basel, Switzerland. A detailed disclosure from each author will be included in the presentation.

EPR-225

Efficacy of Ofatumumab on Microglia in Patients with Relapsing forms of Multiple Sclerosis: Study Design

T. Singhal [1], H. Weiner [1], T. Chitnis [1], R. Bakshi [1], M. Houtchens [1], B. Glanz [1], K. O'Connor [1], J. Ficke [1], E. Rissanen [1], J. Zurawski [1], S. Cicero [1], H. Kropshofer [3], N. Seneca [3], B. Brown [2], M. Ziehn [3]

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Background and aims: Ofatumumab, an FDA approved fully-human anti-CD20 monoclonal antibody, is indicated for the treatment of relapsing forms of multiple sclerosis (RMS) following results from the ASCLEPIOS Phase III trials. However, the potential impact of ofatumumab on microglial activation in MS is unknown. Here we present the design of a study aimed to determine the ofatumumab effect on microglial activation using [F-18]PBR06-positron emission tomography (PET) in RMS patients.

Methods: An open-label, observational, prospective, 9-month study will be conducted in active RMS patients (aged 1,860 years), with evidence of clinical and/or MRI disease activity (Lublin 2014 criteria) and EDSS of 0 to 5.5. Patients will undergo PET and other procedures at baseline and at days 5, 28, 90 and 270 after initiating ofatumumab. The primary objective is to determine the effect of ofatumumab on microglial activation over nine months. Secondary objectives include, time course of effect of ofatumumab on microglial activation and its relationship with peripheral B-cell depletion, serum neurofilament light chain and glial-fibrillary acid protein levels and relationship of PET changes following ofatumumab initiation with 3T MRI changes and clinical parameters.

Results: This is a single-center study in the United States consisting of 10 patients with active RMS. The first patient first visit occurred in October 2020, and the expected study completion is in Q4 2021. The detailed study design will be presented at the congress.

Conclusion: This is the first study to evaluate the effect of ofatumumab on microglial activation and its relationship with serum markers of neurodegeneration and reactive astroglia in RMS patients.

Disclosure: The study was supported by Novartis Pharma AG, Switzerland. The detailed author disclosures will be presented in the subsequent presentation.

EPR-226

Effect of Siponimod on the MSWS-12 and MSIS-29 in Patients With SPMS From the EXPAND Study

J. Hobart [1], D. Piani-Meier [2], B. Cree [3], G. Giovannoni [4], L. Kappos [5], R.J. Fox [6], A. Bar-Or [7], J. Maca [8], S. Arnould [2], G. Karlsson [2], N. Adlard [2], T. Hach [2], R. Gold [9], P. Vermersch [10]

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Background and aims: In the Phase 3 EXPAND study in SPMS, siponimod showed a favourable effect on the 12-item Multiple Sclerosis Walking Scale (MSWS-12). Treatment effects on 29-item Multiple Sclerosis Impact Scale (MSIS-29) and MSWS-12 were further investigated by applying clinically meaningful cut-offs based on literature, in addition to the change from baseline.

Methods: Of 1,651 patients randomised, 1,327 completed the EXPAND core study (median duration, 21 months). Change from baseline for MSIS-29 was assessed using a mixed-effect repeated measures model. Time to 6-month confirmed progression (6m-CP) was assessed using a Cox regression model, with meaningful cut-offs defined as ≥7.5 (MSIS-29) and 4/6/8/10 (MSWS-12) points in the overall population and active/non-active SPMS and age ≤/>45 years subgroups.

Results: In the overall population, increases from baseline in MSIS-29 physical and psychological scores were significantly reduced with siponimod versus placebo (Table 1). Risk of 6m-CP in the MSIS-29 physical score also decreased in the overall population (hazard ratio [HR] 0.78, p=0.0147), active SPMS (0.73, p=0.030) and age ≤45 years (0.63, p=0.005) subgroups. Trends favouring siponimod were observed for 6m-CP in MSIS-29 psychological score. On MSWS-12, pronounced reductions in 6m-CP risk were observed with more stringent cut-offs of 6/8/10 points in the overall population (HR 0.75–0.80, p<0.05), active SPMS (0.72–0.74, p<0.05) and age ≤45 years (0.67–0.71, p<0.05) subgroups.

MSIS-29 physical score

Time point	Siponimod Adjusted mean (SE) (N=1099) (N'=1001)	Placebo Adjusted mean (SE) (N=546) (N'=508)	Difference in adjusted means	Comparison of adjusted means (siponimod vs placebo) SE, 95% CI	p-value
Average over all visits up to Month 30	2.29 (0.62)	4.38 (0.82)	−2.09	0.92 (−3.89; −0.29)	0.0231

MSIS-29 psychological score

Time point	Siponimod Adjusted mean (SE) (N=1099) (N'=998)	Placebo Adjusted mean (SE) (N=546) (N'=506)	Difference in adjusted means	Comparison of adjusted means (siponimod vs placebo) SE, 95% CI	p-value
Average over all visits up to Month 30	0.00 (0.66)	1.98 (0.87)	−1.97	0.98 (−3.89; −0.05)	0.0441

*Pre-specified analyses using a mixed effect repeated-measures model. CI, confidence interval; MSIS-29, 29-item Multiple Sclerosis Impact Scale; MSWS-12, 12-item Multiple Sclerosis Walking Scale; N, number of subjects in the treatment arm; N', number of subjects included in the analysis with at least one result at baseline and after baseline; SE, standard error

Table 1. Change from baseline in MSIS-29 physical and psychological impact scores* (overall study population)

Conclusion: Siponimod reduced the increase in MSIS-29 and MSWS-12 scores and the risk of clinically meaningful confirmed progression in SPMS patients. The effect was more apparent in younger (age ≤45 years) or active SPMS patients.

Disclosure: The study was supported by Novartis Pharma AG, Switzerland. Detailed author disclosures will be provided in the subsequent presentation.

EPR-227

Blood-based metabolomics and MRI parameters in CIS and in RRMS

M.K. Boziki [1], A. Pechlivanis [2], S. Sintila [2], E. Karafoulidou [1], C. Bakirtzis [1], E. Kesidou [1], P. Theotokis [1], G. Theodoridis [2], E. Gkika [2], N. Grigoriadis [3]

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Background and aims: The recognition of a metabolic product associated with autoimmunity in the Central Nervous System (CNS) in peripheral blood samples indicates that it is possible to apply the method for the identification of biomarkers in tissues readily accessible, remote from the CNS. The aim of the present study is to apply blood-based metabolomic analysis in order to discriminate among patients with Clinically Isolated Syndrome (CIS), Relapsing-Remitting Multiple Sclerosis (RRMS) and/or healthy controls and to explore potential associations between metabolomic profiles and MRI parameters.

Methods: Serum samples from 29 MS, 29 CIS and 11 control subjects were analysed using a multitargeted UPLC HILIC-MS/MS method (capable of quantifying 107 polar metabolites). 46 metabolites (mainly aminoacids, central carbon metabolites, sugars) passed the rigorous QC procedure and their values were multivariately correlated and modelled with 167 biochemical and MRI (T1 Volumetry and FLAIR Lesion burden) measurements.

Results: Metabolomic analysis was able to discriminate between RRMS (p-value=8.59858e–005), as well as between CIS patients and healthy controls (p-value= 0.00407416). MRI parameters partly exhibited correlation with disease status, as predicted by metabolomic profiling.

Conclusion: Multivariate models were able to classify accurately MS and CIS samples from controls. Further addition of MRI parameters may increase the discriminating capacity of the blood-based metabolomic model to predict the disease status, thus facilitating more detailed fingerprint profiling for patients with RRMS and CIS.

Disclosure: This research is co-financed by Greece and the European Union (European Social Fund- ESF) through the Operational Programme «Human Resources Development, Education and Lifelong Learning 2014–2020» (MIS5047872)

EPR-228

Thalamic volume is reduced in asymptomatic carriers of the C9ORF72 hexanucleotide repeat expansion

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Background and aims: Carriers of high-risk gene mutations associated with neurodegenerative disease offer an opportunity to discover pre-symptomatic disease markers. A hexanucleotide repeat expansion (HRE) in C9ORF72 is the most common genetic cause of amyotrophic lateral sclerosis (ALS) and the clinicopathologically-linked condition of frontotemporal dementia (FTD). Subcortical structures show atrophy in both ALS and FTD patients. We sought to study this in a cohort of asymptomatic C9ORF72 HRE carriers.

Methods: Participants were recruited from a tertiary ALS referral clinic, consisting of 16 patients diagnosed with ALS, nine asymptomatic gene carriers and 15 healthy controls, which included relatives who tested negative for the C9ORF72 HRE. T1-weighted MRI (1mm isotropic resolution) data were acquired (SIEMENS Prisma 3T). Subcortical structures were segmented using FIRST model-based segmentation from the FMRIB software library and compared across groups using a one-way repeated measures ANOVA with post-hoc unpaired t-tests.

Results: Thalamic volume was significantly reduced bilaterally in both asymptomatic gene carriers and ALS patients compared to controls. Left amygdala volumes were reduced in only the affected ALS patient group.

		Group		
Individual variables		ALS (N=16)	Pre-symptomatic C9+ (N=9)	Control (N=15)
Gender	Male	11	4	7
	Female	5	5	8
Mean Age		55.60	46.77	49.50

Figure 1 – Patient demographics

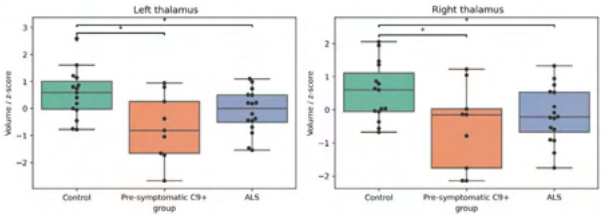

Figure 2 – standardised volume differences between groups: Left and Right thalamus

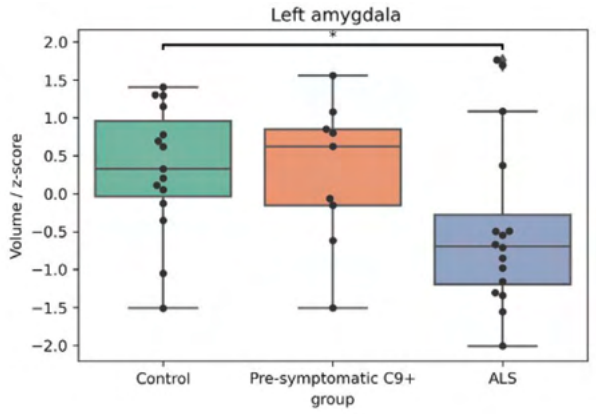

Figure 3 – standardised volume differences between groups: Left amygdala

Conclusion: In line with a study in asymptomatic C9ORF72 HRE carrier relatives of familial FTD patients, our finding of reduced thalamic volume reflects widespread cortical pathology long before the predicted onset of clinical diagnosis in the ALS-FTD continuum. This is a feature of both nervous system redundancy and compensation, and supports a future strategy of earlier therapeutic intervention in high risk patients. More precise mechanistic implications of these changes will be further explored using multimodal imaging data examining thalamic structural and functional connectivity patterns.

Disclosure: Nothing to disclose.

EPR-229

Paramagnetic Rim lesions are associated with progression and disease activity 15 years after a 1st demyelinating event

M. Mossad [1], F. Maizeroi [2], E. Morvan [4], K. Zuber [4], E. Poirion [1], R. Deschamps [1], C. Bensa-Koscher [1], J. Savatovsky [3], A. Moulignier [4], J.-C. Sadik [4], O. Gout [4], A. Gueguen [1]

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Background and aims: Chronic active lesions could be part of mechanism underlying progressive course of MS, since they predominate in progressive patients on pathological studies. Those lesions are surrounded by activated macrophages/microglia, visible on susceptibility weighted imaging MRI sequences as a paramagnetic Rim. This study aims is to describe paramagnetic Rim and their association with disease activity and progression 15 years after a 1st demyelinating event.

Methods: We design a trans-sectional study embed in a prospective cohort of patients followed after a 1st demyelinating event. 116 Patients underwent a 3T brain MRI including 3D FLAIR, 3D SWI and 3D T1 GE and a clinical evaluation to collect EDSS, phenotype and treatment . Cohort follow-up data were used to define disease activity, EDSS worsening and progression in the previous five years. 3D FLAIR, 3D SWI phase and 3D T1 GE were coregistred. MS lesions were manually segmented by two blinded examiners and black holes lesions defined by threshold. Number and volume of paramagnetic Rim, FLAIR and black hole MS lesions were extracted. A multivariate analysis using AIC criteria and backward selection was performed. Correlations were assessed using Spearman tests.

Results: Rim lesions were observed in 4/28 CIS, 33/77 RR-MS, 8/11 SP-MS patients. In multivariate analysis, SP-MS course (OR 4.38 (1.1–22.1), p=0.04) and disease activity (OR 3.32 (1.5–7.8), p=0.005) were factors associated with Rim lesions. Association between Rim lesions volume and Flair / Black holes lesions volume were observed (r=0.31; p=0.04 / r=0.34; p=0.02, respectively).

median [range] mean ± SD n(%)	Total (n=116)	CIS (n=28)	RR (n=77)	SP (n=11)	p (test)	CIS vs. RR	CIS vs. SP	RR vs. SP
Number of relapses	3 [1-20]	1 [1-1]	4 [1-20]	7 [3-15]	p < 0.0001 (K)	p < 0.0001 (W)	p < 0.0001 (W)	p = 0.0617 (W)
EDSS at 15 years	2 [0-8.5]	1 [0-3]	2 [0-6]	6.5 [4.5-8.5]	p < 0.0001(K)	p = 0.0008 (W)	p < 0.0001 (W)	p < 0.0001 (W)
Stratified EDSS at 15 years								
< 3	81 (70.4)	26 (92.9)	55 (72.4)	0	p < 0.0001 (PR)			
>=3 - <6	24 (20)	2 (7.1)	21 (26.3)	1 (9.1)				
≥ 6	11 (9.6)	0	1 (1.3)	10 (90.9)				
Evolution since last 5 years								
Worsening	25 (78.3)	0	18 (23.7)	7 (63.6)	p < 0.0001 (F)			
Clinical activity	37 (31.8)	0	34 (44.2)	3 (27.3)	p < 0.0001 (F)			
Clinical / radiological activity	44 (37.9)	2 (7.1)	37 (48.0)	5 (45.4)	p = 0.0002 (F)			
Progression	10 (8.7)	0	4 (5.26)	6 (54.5)	p < 0.0001 (F)			
Treatment								
None	59 (50.9)	27 (96.4)	23 (29.9)	9 (81.8)	p < 0.0001 (PR)			
1ère line	44 (37.9)	1 (3.6)	43 (55.8)	0				
2ème line	13 (11.2)	0	11 (14.3)	2 (18.2)				

Table 1. Clinical data K : Kruskal-Wallis. W : Wilcoxon pair to pair. F: Fischer. PR: Pearson

median [range] mean ± SD n (%)	RIM - n = 71	RIM + n = 45	p (test) OR (95%IC)
SP course			
yes	3 (27.3)	8 (72.7)	p = 0.01 (PR)
no	68 (64.8)	37 (35.2)	4.9 (1.2 - 19.6)
EDSS at 15 years	2.0 ± 1.7	3.0 ± 1.9	p = 0.002 (K)
EDSS ≥ 3			
yes	15 (44.1)	19 (55.9)	p = 0.01 (PR)
no	56 (69.1)	25 (30.9)	2.8 (1.2 – 6.4)
Evolution since last 5 years			
Worsening			
yes	11 (44)	14 (56)	p = 0.04 (PR)
no	60 (66.7)	30 (33.3)	2.5 (1.0 – 6.3)
Clinical activity			
yes	17 (45.9)	20 (54.1)	p = 0.02 (PR)
no	54 (68.3)	25 (31.7)	2.5 (1.1 – 5.7)
Clinical / radiological activity			
yes	20 (45.4)	24 (54.5)	p = 0.006 (PR)
no	51 (70.8)	21 (29.2)	2.9 (1.3 – 6.3)
Progression			
yes	6 (60)	4 (40)	p = 0.9 (PR)
no	65 (61.9)	40 (38.1)	
Treatment			
yes	32 (56.1)	25 (43.8)	p = 0.27 (PR)
no	39 (66.1)	20 (33.9)	

Table 2. Clinical parameters and presence of paramagnetic rim. RIM±: absence/presence of paramagnetic rim. W : Wilcoxon pair to pair. PR: Pearson

Conclusion: Paramagnetic Rim lesions were associated with progression, disease activity and black holes.
Disclosure: Nothing to disclose.

EPR-230

Neuropsychological assessment in aggressive multiple sclerosis treated with stem cell transplantation

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Background and aims: Autologous haematopoietic stem cell transplantation (AHSCT) induces suppression of clinical-radiological inflammatory activity even in aggressive multiple sclerosis (aMS). However, potential neurotoxicity of the procedure, with possible impact on physical and cognitive disability, has recently been suggested. We present a retrospective analysis evaluating the impact of intermediate-intensity AHSCT on cognitive performances in aMS patients treated at the University-Hospital of Careggi in Florence in the period 2016–2020.
Methods: Haematopoietic stem cells, mobilised with cyclophosphamide and Granulocyte-colony stimulating factor, were reinfused after BEAM+ATG conditioning. The following tests were administered at baseline and follow-up (month 6, 12 and 24) after transplant: symbol-digit modalities test (SDMT), Corsi block-tapping test (CBTT), verbal phonemic and semantic fluency tests (FT). Scores corrected for age, gender and education, and equivalent scores (ES) are reported.
Results: 13 aMS were included (table 1). Assessments at one and two years of follow-up were available for 10 and four cases respectively. Median score in SDMT improved at 12 months compared both to baseline and month six (p=0.011 and 0.018 respectively). No significant variations were observed in CBTT and ES at last follow-up were stable in 9/13 cases (69%), while improved in 3/13 cases (23%) compared to baseline. A trend of improvement was observed in the FT, which reached significance in semantic FT at month six (p=0.017).

	n	(%)
Gender, female	10	(77%)
MS form, relapsing-remitting	8	(61%)
MS form, secondary-progressive	5	(39%)
	median	(range)
Age at AHSCT, years	39	(32 – 48)
Disease duration at AHSCT (from MS onset), years	18	(4 – 29)
Progressive phase duration at AHSCT, months	14	(7 – 79)
Baseline Expanded Disability Status Scale (EDSS)	4.0	(2.0 – 6.5)
Previous treatment duration at AHSCT, years	13	(3 – 22)
Disease modifying treatments received prior to transplant, number	4	(1 – 6)
Education, years	16	(11 – 18)

Table 1: baseline clinical and demographic characteristics of patients affected by aggressive MS included in the study (n=13).

Conclusion: Neuropsychological performance was not impaired by the procedure and a trend to medium/long term improvement was observed, suggesting that AHSCT improves cognitive performance and cognitive fatigue. If any procedure-dependent neurotoxicity developed, it was largely compensated by disease suppression.
Disclosure: Nothing to disclose.

Neurogenetics

EPR-231

Study of genes networks and Mirnas affecting signaling pathways in multiple cognitive impairment and Alzheimer's disease

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Background and aims: Multiple factors contribute to the onset of Mild Cognitive Impairment (MCI) and Alzheimer's disease (AD). The study investigated SNPs regulating interactions among genes and miRNAs that could contribute to MCI and AD physiopathology.
Methods: The study included 371 patients (217 MCI and 154 AD) and 503 control samples representative of the European general population. Open Array technology was utilized to genotype patients for a panel of 120 Single Nucleotide Polymorphisms (SNPs) selected by literature and bioinformatics approaches. Non-coding variants were mostly preferred as they may provide additional knowledge concerning the regulatory gene networks and the biological pathways underlying MCI and AD. Extensive statistical and bioinformatic analysis assessed their association with AD and MCI and identified network of genes and miRNAs relevant to these disorders.
Results: 21 SNPs were associated with MCI risk and 13 SNPs with AD. These variants were mainly located in genes and miRNAs involved in neuroinflammation, neurodegeneration, angiogenesis, formation of amyloid fibrils, memory dysfunction. Some of the genes and miRNAs associated with MCI (IL6, IL7R, INPP5D, MAPK1, STAT3, TNFSF14, SEMA5A, ZMIZ1, CYP24A1, miR-146a, miR-196a, miR499a) and AD (APOE, CLU, SORL1, MAK1, SYT11, LRRK2, IL23R) participate in regulatory networks affecting the signalling cascade of APP, miR-155 and TGB1-TNF-IFNG pathways, which contribute to neuroinflammation and neurodegeneration.
Conclusion: Multiple signaling pathways involved in the physiopathology of MCI and AD could be affected by the networks of genes and miRNA interactions identified in the study, which provided additional knowledge concerning the possible biomarkers and drug targets for these pathologies.
Disclosure: Nothing to declare.

EPR-232

Frequency of C9orf72 mutation among patients diagnosed with neurodegenerative diseases in a Hungarian cohort

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Background and aims: The G4C2 hexanucleotide repeat expansion in the non-coding region of gene C9orf72 was first described in association with amyotrophic lateral sclerosis (ALS) and familial frontotemporal dementia (FTD). Further clinical experiences rose this genetic alteration to the most common genetic role of both familial ALS and FTD. Beside the significance of C9orf72 in ALS-FTD spectra, it was also observed in several other neurodegenerative disorders such as parkinsonism and Huntington-like phenocopies (HDP). Our aim was to establish the frequency of C9orf72 hexanucleotid repeat expansion in a Hungarian caucasian cohort among MND, FTD, Huntington-like and parkinsonian patients.
Methods: We examined 770 Hungarian caucasian patients diagnosed with MND (n=409), dementia (n=159), Huntington-like phenocopy (n=66) or Parkinson syndrome (n=159). In all subjects, the region of C9orf72 containing the hexanucleotid repeat was amplified with repeat primed polymerase chain reaction technique. Samples were analysied with the software GeneMapper 4.1. paired against healty and affected controls.
Results: Out of the 770 patients tested 60 had pathologic hexanucleotid repeat expansion (>30 repeats). Positive results made up 8,5% of MND, 5,6% of dementia, 7,5% of HDP and 2,2% of the parkinsonian group.
Conclusion: Pathologic C9orf72 hexanucleotid expansion was found in a combined 5,95% of a cohort with MND, FTD, Huntigton-like phenocopy and parkinsonism. Our result implies this genetic alteration can be found in several neurodegenerative disorders which indeed might form a spectra rather being distinct entities or points to a common pathophysiological process.
Disclosure: Two authors of this publication are members of the European Reference Network for Rare Neurological Diseases – Project ID No 739510.

EPR-233

The electrophysiological footprint of CACNA1A disorders

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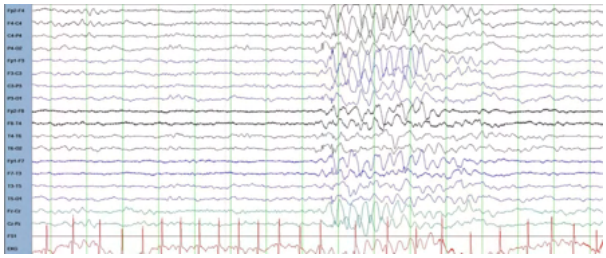
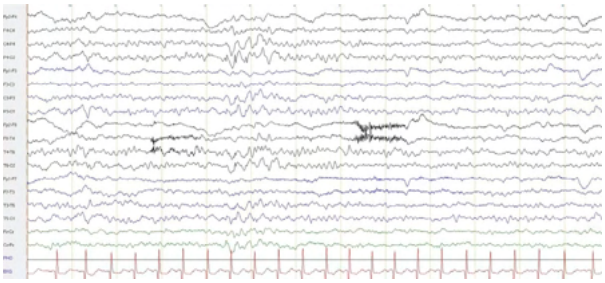
Background and aims: CACNA1A variants underlie three neurological disorders: familial hemiplegic migraine type 1 (FHM1), episodic ataxia type 2 (EA2) and spinocerebellar ataxia type 6 (SCA6). EEG is applied to study their episodic manifestations, but findings in the intervals did not gain attention up to date.

Methods: We analyzed repeated EEG recordings performed between 1994 and 2019 in a large cohort of genetically confirmed CACNA1A patients. EEG findings were compared with those of CACNA1A-negative phenocopies. A review of the related literature was performed.

Results: 85 EEG recordings from 38 patients (19 EA2, 14 FHM1, five SCA6) were analyzed. Baseline EEG was abnormal in 55% of cases (12 EA2, nine FHM1). The most common finding was a lateralized intermittent slowing, mainly affecting the temporal region. Slowing was more pronounced after a recent attack but was consistently detected in the majority of patients also during the follow-up. Interictal epileptic discharges (IEDs) were detected in eight patients (7 EA2,1 FHM1). EEG abnormalities and especially IEDs were significantly associated with younger age at examination (16±9 vs 43±21 years in those without epileptic changes, p=0.003) and with earlier onset of disease (1(1–2) vs 12(5–45)years, p=0.0009). EEG findings in CACNA1A-negative phenocopies (n=15) were largely unremarkable (p=0.03 in the comparison with CACNA1A patients).



Superimposed bilateral occipital spikes in generalized rhythmic Delta activity in a child with EA2. Bipolar longitudinal montage with 70 Hz filter and time constant of 0.3 s; sensitivity 10 V.



Superimposed bilateral occipital spikes in generalized rhythmic Delta activity in a child with EA2. Bipolar longitudinal montage with 70 Hz filter and time constant of 0.3 s; sensitivity 10 V.

Conclusion: EEG abnormalities between attacks are highly prevalent in episodic CACNA1A disorders and especially associated with younger age at examination and earlier disease onset. Our findings underpin an age-dependent effect of CACNA1A variants, with a more severe impairment when P/Q channel dysfunction manifests early in life.

Disclosure: No funding or competing interests related to the present work.

EPR-234

The role of the C9ORF72 hexanucleotide repeat size in dementia

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Background and aims: The hexanucleotide repeat expansion (RE) in the C9ORF72 (chromosome 9 open reading frame 72) gene is the most common genetic cause of amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD). A reading length in the order of thousands occur in symptomatic mutation carriers, who can also present with other neurodegenerative disorders. The cut-off between normal and pathogenic alleles is not well established. Repeat sizes larger than in controls but not enough to cause disease are called intermediate repeats and further studies are needed to better understand their role in neurodegeneration. In this study, we screened our dementia cohort in order to gain further insight into the prevalence and impact of the C9ORF72 variant.
Methods: DNA derived from patients and unaffected individuals was obtained from the Department of Neurology of the Medical University of Vienna (n= 747), the PRODEM collective (n=510) and the VITA collective (n=154). Genotyping was performed using a two-step PCR assay followed by Southern blotting to estimate the repeat length.
Results: In our cohort, 5.4% of behavioral FTD and 1% of Alzheimer's disease (AD) cases (0.4% late and 3.5% early onset AD) are carriers of the C9ORF72 RE. Intermediate repeat alleles were associated with cerebellar symptoms ($p<0.01$, OR=4.4), especially in carriers of two intermediate alleles ($p<0.05$, OR=8.5).
Conclusion: C9orf72 RE occur in a remarkably high proportion of patients with early onset AD, highlighting the importance of screening for this variant in this group of patients. Furthermore, our results suggest that C9ORF72 intermediate repeats might act as disease modifiers.
Disclosure: All authors declare no conflicts of interest.

EPR-235

Delineation of epileptic and neurodevelopmental phenotypes associated with STX1B

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Background and aims: We aim to further delineate the clinical and genetic spectrum of epileptic and neurodevelopmental conditions associated with variants in STX1B.

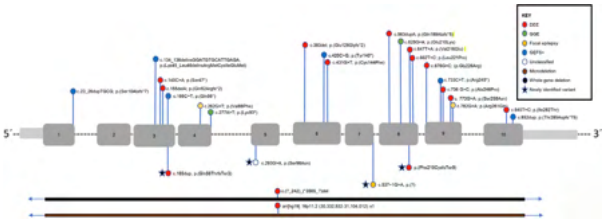

Figure 1. Overview of pathogenic and likely pathogenic variants in STX1B.

Methods: We screened our diagnostic in-house database (comprising >20,000 exome sequencing datasets) for pathogenic and likely pathogenic variants in STX1B. The detected cases were phenotyped in detail, and the findings were compared to previously published patients.
Results: We identified four unrelated individuals with pathogenic or likely pathogenic variants in STX1B (one missense and three loss-of-function variants). All patients displayed epileptic phenotypes, including epileptiform discharges on electroencephalography (without apparent seizures), developmental and epileptic encephalopathy and focal epilepsy. three of the four patients had developmental delay. Febrile seizures occurred in two individuals. One patient with focal epilepsy underwent epilepsy surgery without lasting improvement. The neuropathological workup of brain tissue revealed a mild malformation of cortical development (i.e., subtle subcortical heterotopia).

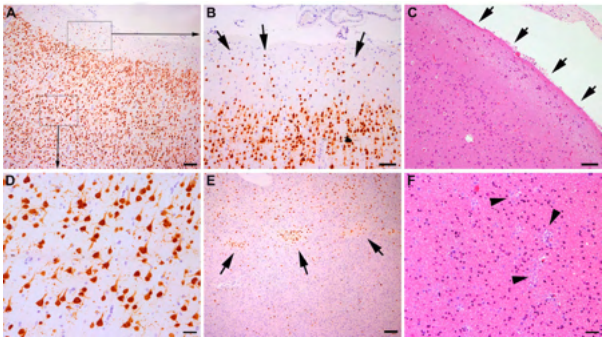

Figure 2. Neuropathological workup of resected temporal lobe tissue in STX1B-related focal epilepsy (Patient 3) showing a mild malformation of cortical development.

Conclusion: Our findings confirm the wide clinical range of STX1B-related epileptic conditions and include subtle neuronal migration disorders in its phenotype spectrum. The identification of loss-of-function variants in very differently affected individuals suggests that no clear genotype-phenotype correlation can be established.
Disclosure: Nothing to disclose.

EPR-236

Late-onset ataxia due to RFC1 repeat expansion: a multicentric national study

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Background and aims: RFC1 repeat expansion was recently identified as a cause of CANVAS (cerebellar ataxia, neuropathy and vestibular areflexia syndrome) and sporadic idiopathic late-onset ataxia (ILOCA). As RCF1 genetic defects emerge as a major cause of ILOCA, detailed clinical characterization is fundamental for the correct definition of its phenotypic spectrum.

Methods: Phenotypic characterization of a population with RFC1 expansion. Revision of electronic medical records and RFC1 repeat expansion screening.

Results: Included 35 patients, 11 belonged to four families, and of the remaining 24, 8 had family history of ataxia. The median age of neurological manifestations was 59±10 years. The most common symptoms at presentation were gait imbalance (n=33) and sensory symptoms (n=16). Cough, reported by 66% (n=23), started between the 3rd and 7th decades of life. Six patients reported cough improvement with progression of the ataxia. All patients developed sensory neuropathy and 69% (n=24) had full CANVAS. Two patients had pyramidal signs (distal paresis with spasticity), two auditory and one optic tracts involvement, and two developed ileus paraliticus. Cerebellum atrophy in brain MRI occurred in 19 patients (63%).

Conclusion: This paper explores the phenotypic spectrum of repeat expansions in RFC1 in our 1st 35 genetically confirmed patients, enrolled from multiple centres from Portugal. The phenotype of our cohort is generally similar to previously descriptions, being the sensory neuropathy an universal component. We found an inverse relationship between cough and ataxia severity. Pyramidal, auditory and optic tracts involvement and severe dysautonomia were identified in patients of our cohort, expanding the phenotypic heterogeneity of RFC1.

Disclosure: N/A

Neuroimaging 1

EPR-237

Does the Anna Karenina principle apply to vestibular migraine and Meniere's disease?

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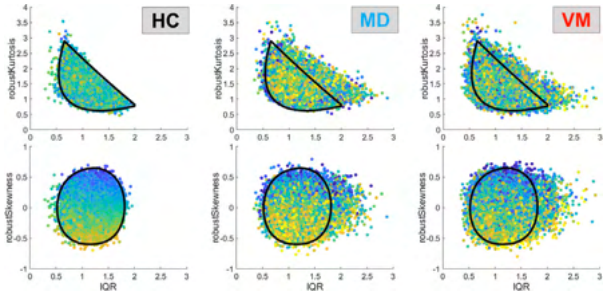
Background and aims: It is unclear how Meniere's disease (MD) and vestibular migraine (VM), which often appear in clinically similar attacks, differ from healthy controls (HC) in functional connectivity, especially during the interictal phase. The central functional connectivity feature of VM and MD might be "disorganization" relative to HC, due to unpredictable attacks that cannot be compensated for. This "Anna Karenina principle" states that all HCs are very alike while all patients are very dissimilar from each other and the HCs. Here we examined the distribution parameters of functional connectivity between HC, VM and MD to elucidate the state of disorganization in the interictal phase.
Methods: 50 HCs and 93 patients (42 VM, 51 MD) underwent fMRI while resting in a 3T MRI (Siemens). Resting-state fMRI connectivity measures were extracted via dual regression and normalized in mean and standard deviation relative to HCs. Robust distribution parameters for all voxels in the grey matter were compared between groups.
Results: Distribution parameters were compact for HCs, while those of VM and MD patient groups were significantly more dispersed, i.e., disorganized (Fig 1). In figure 1 the bulk of values for the HCs were marked by black outline and superimposed onto the values for the MD and VM groups.



Distribution parameters per voxel. Color of dots indicates the robust skewness from -1 to 1 (blue to yellow). Values for healthy controls (HC) were marked with a black line and superimposed on Meniere disease (MD) and vestibular migraine (VM) group data.

Conclusion: Resting-state functional connectivity measures imply disorganized interactions between patients relative to HCs, even in the interictal phase. VM and MD patients are very different in functional connectivity, suggesting that the Anna Karenina principle might apply to these patients.
Disclosure: We have no conflict of interest to disclose with regard to this subject matter.

EPR-238

Comparison of In Vivo and Ex Vivo MRI in a Rat Model for Glioblastoma

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Background and aims: Glioblastomas represent the most common and aggressive malignant primary brain tumors in adults. Magnetic resonance imaging (MRI) plays an important role in outcome measurement in a preclinical setting. Visual discrimination between tumor tissue and tumor-associated tissue changes is challenging. We compared anatomical changes in a glioblastoma animal model using in vivo MRI, ex vivo MRI and histology.
Methods: 18 rats were inoculated with 20000 F98 cells in the right entorhinal cortex. In vivo MRI (T2 and diffusion tensor imaging (DTI)) was performed at day 10 in 6/18 animals, followed by transcardial perfusion, ex vivo MRI (T2) and histology in all 18 animals.
Results: A significant difference in volumes of signal intensity changes between in vivo and ex vivo T2 was found ($p<0.01$). Volumes determined on ex vivo T2 were comparable to histological tumor volumes. On in vivo mean diffusivity (MD) images (derived from DTI), tumors were displayed as an outer rim of more hyperintense signal with a core of hypointense signal. Volumes of the hypointense core on in vivo MD images were comparable to histological tumor volumes.
Conclusion: As signal intensity changes on ex vivo T2 MRI were approximately four times smaller compared to in vivo T2 MRI, but comparable to histological tumor volumes, these changes most likely reflect actual tumor volumes, whereas changes on in vivo T2 MRI probably include peritumoral edema and reactive gliosis. MD images display tumors as two regions with distinct intensities and might be used in future to distinguish tumors from tumor-associated tissue changes in preclinical models.
Disclosure: Charlotte Bouckaert is supported by a junior researcher ('Aspirant') grant from the "Fonds voor Wetenschappelijk Onderzoek (FWO)"

EPR-239

Dynamic functional connectivity changes of thalamic sub-regions underpin disability in multiple sclerosis

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Background and aims: Thalamic sub-regions (frontal, motor, occipital, post-central and temporal) have distinct resting state (RS) functional connectivity (FC) profiles. Although static inter-, intra- and cortico-thalamic RS FC changes were described in multiple sclerosis (MS) patients, dynamic FC (dFC) analyses may reveal further pathological abnormalities underpinning clinical disability. Here, we explored abnormalities of sub-regional thalamic dFC characterizing MS patients.

Methods: 89 MS patients (49 relapsing-remitting [RR]; 40 progressive [P]MS) and 53 healthy controls (HCs) underwent RS fMRI, clinical disability and neuropsychological assessment. Thalamic sub-regional dFC was quantified using sliding-window seed-voxel correlation analysis. Standard deviation (SD) of dFC across windows was taken as dynamicity measure. Between-group comparisons and correlations with disability were assessed with voxel-wise ANOVA, t-Tests and linear regressions.

Results: MS patients showed an overall dFC decrease between most thalamic sub-regions and fronto-temporo-occipital regions vs HCs, which was mainly driven by RRMS. PMS patients exhibited lower dFC than HCs between fronto-occipital thalamic sub-regions and occipito-parietal cortices; however, they also showed higher SD between almost all thalamic sub-regions and fronto-temporal areas. Cognitive impairment was associated with higher SD between all sub-thalamic regions and areas belonging to default-mode and sensory-motor networks. Higher clinical disability correlated with increased dFC of frontal, motor and post-central thalamic sub-regions with contralateral thalamus and fronto-temporal cortices.

Conclusion: RRMS patients experienced reduced dFC vs HCs. On the other hand, PMS patients as well as patients with cognitive impairment and higher disability had increased thalamo-cortical FC dynamicity. Increased dFC may reflect maladaptive mechanisms related to disease pathology.

Disclosure: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

EPR-240

Diagnostic accuracy of QyScore® MRI markers in the clinical spectrum of Alzheimer's disease

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Qynapse, Paris, France

Background and aims: Diagnostic criteria for Alzheimer's disease (AD) acknowledge a key role of imaging markers of medial temporal lobe structures, such as hippocampus and amygdala, for early diagnosis. The aim of the present study is to assess the diagnostic accuracy of QyScore® medial temporal lobe atrophy markers in distinguishing AD dementia and Mild Cognitive Impairment (MCI) individuals from healthy controls (HC) in US and EU cohorts.

Methods: 3DT1 images were selected from different cohorts (ADNI, MEMORA, NACC, OASIS3) and analysed using the QyScore® automatic segmentation pipeline. Brain volumes of hippocampus ad amygdala were normalized to the total intracranial volume. Analyses of variance were performed to compare volumetric measurements among clinical groups. Areas under the curve were calculated to identify the diagnostic accuracy of QyScore® markers in discriminating AD and MCI from HC.

Results: The sample was composed of 425 AD, 909 MCI and 993 HC with a higher prevalence of men and Apoe 4 carriers in each group. Analysis of variance showed a significant difference in hippocampal and amygdala volumes among groups. Area under the curve (AUC) showed a good diagnostic accuracy in discriminating AD vs HC and MCI versus HC both for the hippocampal volumes (ADvsHC: AUC=0.86, 95%CI: 0.832–0.877; MCIvsHC: AUC=0.75, 95%Ci: 0.726–0.770), and the amygdala volumes (ADvsHC: AUC=0.77, 95%CI: 0.737–0.791; MCIvsHC: AUC=0.70, 95%CI 95%: 0.675-–0.720).

Conclusion: Our results highlight the good diagnostic performance of QyScore ® markers and support the relevance of implementing these markers in the diagnostic workflow of AD and MCI patients.

Disclosure: Data used for the present study come from the Alzheimer's disease Neuroimaging Initiatives (ADNI) and the National Alzheimer Coordinating Center (NACC) and OASIS3

EPR-241

The Utility of Doppler Ultrasonography in the Study of Lacunar Stroke

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Background and aims: Doppler ultrasonography (DUS) is largely used in the aetiological investigation of ischemic sroke and its subtypes, like lacunar stroke. However, although it is known that the increase in the Pulsatility Index (PI) is associated with small vessel disease (SVD), little is known about the usefulness of this parameter.
Methods: Data were collected from patients with lacunar stroke who underwent DUS (performed a maximum of five days after the event) at an ultrasonography laboratory between January and July 2020. Continuous variables were evaluated using t-tests for independent samples or non-parametric tests, depending on the normality of the distribution. Linear correlation was used to evaluate the association between continuous and/or discrete variables.
Results: Data were obtained from 52 patients, 16 women and 36 men, mean age of 68.5 years. The PI of the middle cerebral artery (MCA), excluding patients with intracranial stenosis of the MCA (five patients), correlated linearly with the severity of white matter changes on the Age-Related White Matter Change (ARWMC) scale, explaining 16.3% of the variation by this model. Concerning vascular risk factors, the PIs of the left internal carotid artery, of the MCAs and the posterior cerebral arteries (PCA) correlated with diabetes and those of the PCA with dyslipidemia ($p < 0.05$).
Conclusion: PI measurement can potentially be useful in assessing SVD causality in lacunar stroke. We propose that this parameter can help to better select patients who will benefit from further aetiological study. Furthermore, this study also suggests that different vascular risk factors affect differently the anterior and posterior circulations.
Disclosure: The authors declare that they have no conflict of interest.

EPR-242

Intravenous delayed Gadolinium-enhanced MR imaging of the endolymphatic space: A methodical comparative study

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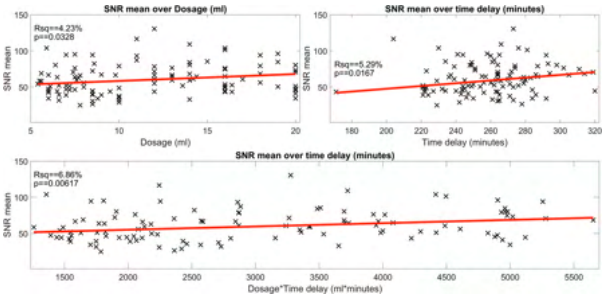
[1] Department of Neurology, Munich, Germany, [2] German Center for Vertigo and Balance Disorders, Munich, Germany, [3] Radiology, Toronto, Canada

Background and aims: Verification of endolymphatic hydrops (ELH) via intravenous delayed Gadolinium (Gd) enhanced magnetic resonance imaging of the inner ear (iMRI) is developing into a standard clinical tool to investigate vestibulo-cochlear syndromes.
Methods: 108 participants, 75 patients with Meniere's disease (MD; 55.2±14.9 years) and 33 vestibular healthy controls (HC; 46.4±15.6 years) were included to examine how (i) MR acquisition protocols influence the signal within endolymphatic space (ELS); (ii) ELS quantification methods correlate to each other and clinical data; and finally, (iii) ELS extent influences MR-signals.
Results: Within 0.1 to 0.2mmol/kg Gd dosage and 4h±30 min time delay, semi-quantitative (SQ) and 2D- or 3D-quantifications of the ELS were independent of signal intensity (SI) and signal-to-noise ratio (SNR) (FWE corrected, $p<0.05$, Figure 1). Used methods correlated strongly (0.3–0.8) and were highly reproducible across raters, thresholds. 3D-quantifications showed least variability. Asymmetry indices and normalized ELH were most useful for predicting quantitative clinical data. ELH size influenced SI, but not SNR. SI could not predict the presence of ELH.



Influence of gadolinium (Gd) dosage and Gd time delay on the signal-to-noise ratio (SNR), (belonging to question i).

Conclusion: 1) Gd dosage of 0.1–0.2mmol/kg after 4h±30 min time delay suffices for ELS quantification. 2) A clinical SQ grading classification including a standardized level of evaluation reconstructed to anatomical fixpoints is needed. 3) ELS 3D-quantification methods are best suited for correlations with clinical variables, should include both ears and ELS values reported relative or normalized to size. 4) ELH leads to mild SI increases. However, these signal changes cannot be used to predict the presence of ELH.
Disclosure: The authors have no conflicts of interest to disclose.

Education and Ethics in neurology

EPR-243

Should we enhance undergraduate education in dementia?

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Background and aims: Due to the growing number of older people with dementia worldwide, an increasing number of people will participate in their care, so do health professionals. The main goal of this research was to get an insight into the level of knowledge and attitudes towards dementia among medical students.
Methods: This is a cross-sectional study. A total of 231 final-year medical students at the School of Medicine, University of Zagreb were recruited. The paper-and-pencil questionnaire included six categories of questions on demographic data (I.), success during medical studies (II.), personal interests (III.), personal attitudes towards dementia and experiences with people with dementia (IV.), two dementia knowledge exams (V.) and personal opinion on the prevalence of dementia in the undergraduate curriculum (VI.).
Results: Students had relatively neutral attitudes towards working with people with dementia and a rather poor theoretical knowledge of dementia. The best theoretical knowledge was about the symptoms of dementia, and the weakest were in the field of differential diagnoses, epidemiology and pathogenesis of dementia. Every 11th final-year medical student had never had contact with a person with dementia. Medical students should spend more time with people with dementia during their medical education was predominant opinion. The higher grade point average in the study and the higher grade in Neurology were significantly correlated to the better result on the dementia knowledge exam.

Table 1. Medians (Mdn), Interquartile Ranges (IQR) and ranges of selected variables.

Variable	Mdn	IQR	Range
Attitudes towards dementia score	38.0	7.0	25-58
Score on 23-MCQ Dementia Knowledge Test	13.0	5.0	2-20
ADKS scores	22.0	4.0	11-28

23-MCQ Dementia Knowledge Test (max score 23)
ADKS - Alzheimer's Disease Knowledge Test (max score 30)

Table 1

Table 2. Dementia knowledge based on the categories of questions

Question category	Mdn	IQR
Clinical Features	0.75	0.25
Risk Factors	0.50	0.50
Treatment	0.60	0.40
Diagnosis	0.25	0.25
Differential Diagnosis	0.0	0.50
Epidemiology	0.0	0.0
Pathogenesis	0.0	0.0

Mdn - median; IQR - Interquartile Ranges

Table 2

Table 3. Spearman correlation coefficients

	Grade Point Average	Grade in Neurology
23-MCQ Dementia Knowledge Test scores	0.218*	0.311**
ADKS scores	0.018	0.007

23-MCQ Dementia Knowledge Test (max score 23); ADKS - Alzheimer's Disease Knowledge Test (max score 30)
*p = 0.001, **p < 0.001

Table 3

Conclusion: There is the need to broaden the current educational program in dementia from the earliest student days in order to increse knowledge and attitudes towards dementia.
Disclosure: The authors report no conflict of interest.

EPR-244

A Framework for Assessing Neurological Data Repositories for Use in Europe

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Background and aims: While Neurologists have long shared data Web-based data repositories have the potential to enable research with large data quantities from multiple sources. Publication of data with journal articles is encouraged by grant funding agencies. Neurologists typically are not trained for informed data consumption nor about impactful data contribution methods. Locating relevant databases and assessing the data quality for clinical use are significant challenges. Data from non-European sources may be unsuitable for use here and data submitted to external databases may erode patient and neurologist protections.
Methods: We coupled information science methods to assess data sources with the domain knowledge of Neurology for meaningful use of external data in medical settings. We conducted this research in three phases: data repository location, repository assessment, and development of guidelines, using online registries, systematic Web searches. We recorded key criteria about infrastructure (location, host, funding, data volume, use/submission policies) and datasets (organism, disorder, instrument, data formats, levels). Using Neurology experience, we compared this with the necessary information reliably using data in a clinical or research setting.
Results: Of 80 Neuroscience data repositories, 52 are located in the USA. EU countries together host 18 repositories. Online databases are difficult to locate. Datasets do not describe critical aspects, which can affect data integration, potentially limiting the quantity of data and thus, the significance of results based on these data.
Conclusion: We have developed a framework to help Neurologists in selecting repositories for submission and guidelines for evaluating public data for use in their work.
Disclosure: This research has not been directly supported by any corporation or agency.

EPR-245

Digital post-graduate paediatric neurology training in the pandemic era

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Background and aims: The British Paediatric Neurology Association (BPNA) run a distance learning (DL) epilepsy module, designed for small group teaching and discussion. The aim of this study was to review the feasibility of running the BPNA epilepsy DL module sessions digitally.
Methods: 16 paediatricians attended 26 weeks of one-hour online sessions. These consisted of participant led presentations followed by group discussions, chaired by a paediatric neurologist. On completion, a feedback survey was sent to participants.
Results: 75% (12/16) of participants completed the survey. 50% (6/12) were paediatric neurology trainees, 25% (3/12) were trainees with epilepsy special interest, 8% (1/12) was a consultant paediatrician and the remainder were paediatricians in non-training posts. 58% (7/12) reported a significant increase in knowledge on managing epilepsy. 67% (8/12) reported the sessions were at the appropriate level. 99% (11/12) attended all or most sessions with 75% (9%) citing on call commitments as a barrier to attending. The discussions were reported to encourage 'critical thinking'. 83% (10/16) respondents felt the learning outweighed the impact on life. All respondents would recommend this format to colleagues, but commented that having recordings of the sessions, and ability to bring personal cases for discussions would be useful. A respondent was concerned that their 'questions would be trivial,' but reported they 'felt welcomed' and 'found the whole team very supportive and approachable'.
Conclusion: The feedback supports feasibility for digital delivery of DL. The format has the potential to develop skills in teaching, listening and debating constructively; important for the future clinician-teachers in paediatric neurology.
Disclosure: Nothing to disclose.

EPR-246

Prognosis, decision making and managing uncertainty in acute ischemic stroke: qualitative study among physicians

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Background and aims: Ischemic stroke is a leading cause of disability and mortality worldwide. As acute stroke patients often lose decisional capacity, the acute situation is fraught with complicated and sometimes conflictive decision making between the patients' relatives and clinicians. We aimed to explore the medico-ethical challenges with regard to three essential elements of acute stroke care: prognosis, decision-making and management of uncertainty.

Methods: Four focus groups were conducted; two in a university hospital and two in a regional hospital. 21 physicians (13 residents and fellows and eight attending physicians), working in neurology and neuro-rehabilitation, participated. The discussions were audio-recorded and transcribed verbatim. Transcripts were analysed thematically according to Braun and Clarke's (2006) reflexive thematic analysis guidelines. Two of the four transcripts were double-coded to establish consistency in the coding framework.

Results: We identified multiple reasons for prognostic uncertainty, arising from limitations in the available information and processes. While multiple tools for improving prognostication seem available, these were not commonly used in clinical practice. In decision making, physicians make use of prudential judgement and affective forecasting. In both prognostication and decision making, time plays a crucial role. We found evidence for a major role of cognitive biases, along with strategies for dealing with this uncertainty, communicating with families and in promoting shared decision making.

Conclusion: The results highlight opportunities to improve stroke care through use of prognostic tools and the need to develop communication strategies for discussing uncertainly, goal-concordant care and promoting shared decision making with patients and families.

Disclosure: Nothing to disclose.

Ageing and dementia 5

EPR-247

RFMRI in patients with unresponsive wakefulness syndrome and minimally conscious state. Preliminary results.

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Background and aims: FMRI at rest allows to evaluate the basic activity of the brain in the absence of stimuli. This technique opens up possibilities for studying functional connectivity of the brain in patients who cannot perform any tasks to learn about their brain functional state.
Methods: 14 patients with disorders of conciousness (DOC) admitted in neurology department underwent resting state fMRI. Subjects were divided into two groups: group 1–8 patients in UWS, group 2–6 patients with minimally conscious state-plus (MCS+). The groups were comparable on age and duration of state. All patients underwent resting state functional MRI. We analyzed the data by performing an intergroup statistical analysis with the medial prefrontal cortex (MPFC) as region of interest.
Results: The number of maps of spontaneous activity were reduced both in UWS and MCS+ patients. Analysis of each resting state network showed that the default mode network (DMN) accurately distinguishes patients in a locked state from patients with a vegetative state. A decrease in activity in the DMN of the brain has been noted in patients with UWS comparing to MCS+. In some cases it was noted that degree of involvement of precuneus network allows for a differential diagnosis between the UWS and the MCS+.
Conclusion: The study of connectome provides new approaches to the analysis of integrative brain function, and to assessment of the treatment effect. RFMRI can be used in patients with impaired consciousness to control the functional activity of the brain.
Disclosure: The study is supported by the grant of the RFFR 19-29-01066

EPR-248

Time to Diagnosis in Young Onset Alzheimer's disease in Central Norway: a Population-based Study

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Background and aims: Young onset dementia is associated with delayed diagnosis, possibly due to heterogeneity and atypical presentation. Our hypothesis was that even the commonest variant of Alzheimer's disease is associated with a substantial diagnostic delay in patients <65 years.
Methods: The main sources of patients were the databases at the Department of Neurology, University Hospital of Trondheim, and the Department of Psychiatry, Levanger Hospital. Other sources included key persons in the communities, collaborating hospital departments, and review of hospital records. Caregivers were interviewed by telephone.
Results: Time from first symptom to diagnosis in typical young onset Alzheimer's disease was 5.5 years (n=223). Time from onset to contact with healthcare services was 3.4 years. Time from contact with healthcare services to the first visit at a hospital was 10.3 months. Time from 1st visit at a hospital to diagnosis was 14.8 months. MRI, CERAD ten-item word test and the analysis of CSF core biomarkers were conducted with a delay of 4.3, 6.5 and 8.3 months, respectively.
Conclusion: Even the commonest presentation of Alzheimer's disease is associated with a substantial diagnostic delay in younger patients. The duration of the disease before patients, or others contact medical services, as well as the overall time to diagnosis, are substantially longer than previously reported. General practitioners may postpone the referral to specialist evaluation. There is a significant delay to the analysis of CSF core biomarkers at hospitals. Public awareness, early referrals, and a speedy analysis of CSF core biomarkers might decrease the diagnostic delay.
Disclosure: Nothing to disclose.

EPR-249

Anti-LGI1 antibody mediated encephalitis may mimic dementia with Lewy Bodies: report of a case

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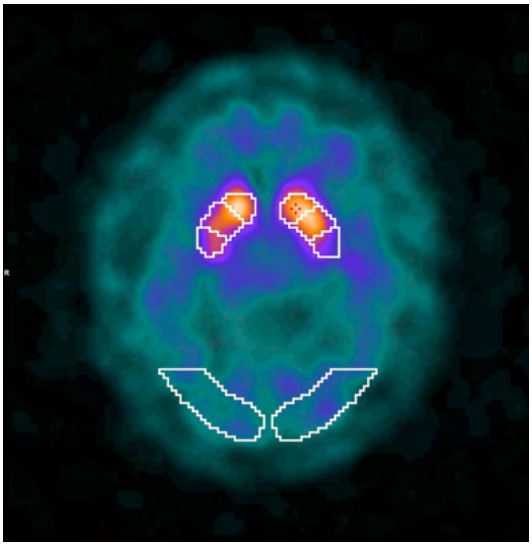
Background and aims: Anti-LGI1 antibody encephalitis may cause cognitive dysfunction, usually showing a good response to immunotherapy. We present a case of rapid progressive dementia that included autoimmune encephalitis and dementia with Lewy Bodies in differential diagnosis.
Methods: A 69-year-old man with prior history of thyroidectomy due to Graves' disease and prostate cancer in complete remission presented with eight months history of progressive cognitive impairment. He showed fluctuating cognition with disinhibition, aggressiveness, hyperphagia, spatial disorientation and altered immediate and delayed memory. He associated visual hallucinations, orthostatism without parkinsonism, and daily paroxysmal episodes lasting a few seconds of unresponsiveness with hyperventilation and tonic flexion of upper limbs.
Results: Blood tests showed hyponatremia and an inflammatory pattern with elevated IgM. CSF analysis showed elevated proteins with elevated IgM and IgG and oligoclonal bands. 14.3.3 protein and Alzheimer's disease markers were negative. A brain MRI revealed global atrophy, with posterior left hypometabolism on brain 18F-FDG PET and DaTSCAN showed decreased uptake in the bilateral putamen. Polysomnography ruled out REM sleep behavior disorder and video-EEG monitoring registered multiple focal seizures of left hemispheric origin. After positive results for anti-LGI1 antibodies in CSF, intravenous immunoglobulins and mycophenolate were started with clinical improvement. Tumor screening showed no significant findings.



DaTSCAN showing bilateral putamen decreased uptake.

Conclusion: This case highlights the possible clinical overlap between degenerative and autoimmune causes of rapidly progressive dementia. A careful diagnosis is mandatory due to prognostic and therapeutic differences between both etiologies.
Disclosure: Nothing to disclose.

EPR-250

FYN, SARS-CoV-2, and IFITM3 in the Neurobiology of Alzheimer's disease

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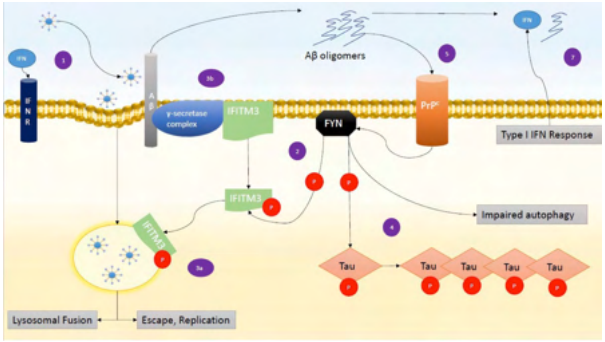
Background and aims: In a previous study, we had detected perturbations in IFITM3 networks in both the CNS and peripheral immune cells donated by AD patients.The purpose of this study is to explore the transcriptomic evidence of the SARS-CoV-2 - AD interplay by exploring perturbations in FYN and IFITM3 gene expression.
Methods: Exploratory analyses involved meta-analysis of bulk and single cell RNA data for IFITM3 and FYN differential expression. For confirmatory analyses, we performed gene set enrichment analysis (GSEA) on an AD gene signature from AD Consensus transcriptomics; using the Enrichr platform, we scrutinized COVID-19 datasets for significant, overlapping enriched biological networks.
Results: Bulk RNA data analysis revealed that IFITM3 and FYN were differentially expressed in two CNS regions in AD: the temporal cortex (AD vs. Controls, adj.p-value=1.3e−-6) and the parahippocampal cortex (AD vs. controls, adj.p-value=0.012). Correspondingly, single cell RNA analysis of IFITM3 and FYN revealed that it was differentially expressed in neuronal cells donated from AD patients (astrocytes, microglia and oligodendrocyte precursor cells), when compared to controls.



A comprehenvsive model

Conclusion: IFITM3 and by extent FYN were found as interactors within biological networks overlapping between AD and SARS-CoV-2 infection. SARS-CoV-2 SARS-CoV-2-mediated IFITM3 induction would mechanistically result in increased A production. FYN recruitment by viral processes results in abrogation of both fusion of IFITM3 vesicles with lysosomes; immunoevasion, by FYN-mediated impairment of autophagy would then serve to promote impaired detoxification from A, while propagating Tau pathology in an IFITM3-independent manner.
Disclosure: Nothing to declare.

EPR-251

SARS CoV2-encephalopathy with focal presentation. A CASE SERIES

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Background and aims: SARS CoV2 encephalopathy is now a recognized entity. We present five cases of encephalopathy associated with SARS CoV2 with focal presentation.
Methods: Case series
Results: Five patients were included (4 males and one woman), mean age was 60 (58–76). Four patients required mechanical ventilation. The clinical presentation were aphasia (3/5), hemianopia (1/5), hemiparesis (1/5) and akinetic mutism (1/5) Metabolic disturbances and vascular etiology were ruled out. Neuroimaging with cranial CT with CT angiography or MRi was performed in all cases. In 3/5 CNS lumbar puncture was performed, showing mirror pattern oligoclonal bands in all of them. The clinic progressively improved until it disappeared in all of them.
Conclusion: SARS CoV2 encephalopathy may present with focal symptoms. More studies are needed to elucidate its pathogenesis. As possible explanations, we propose inflammatory activation at the CNS level, sustained hypoxia. Direct CNS invasion seems less probable.
Disclosure: Nothing to disclose.

EPR-252

Mindset4Dementia: A feasibility trial of an iPhone-based dementia screening application

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Background and aims: The current global rate of undiagnosed individuals with dementia is 62%. We sought to develop an iPhone-based dementia screening application named Mindset4Dementia and assess its feasibility of use in the target population.

Methods: Public Engagement: Early and ongoing interaction with elderly and cognitively impaired groups informed accessible design. The application was submitted for free download on the Apple App Store for three months, and downloads were generated via social and conventional media.

Design: Mindset4Dementia uses a conversational user interface to lead the user through a targeted history and cognitive assessments including modified Stroop and Symbol Digit Modalities tests. Facial recognition and handwriting analysis were incorporated within the design. Regulation: Terms of use were summarised in a concise single-screen summary to ensure informed consent. Expert legal advisors were consulted to ensure compliance with the necessary regulatory bodies.

Results: Mindset4Dementia attained 4,605 full uses, with an average user age of 49.6 years. Users were willing to disclose symptoms and risk factors for dementia (Table 1). An optional feedback survey was completed by 1,240 individuals, who rated the design and build of the application as 90%. Additionally, 92% noted a desire to integrate Mindset4Dementia in their national health system, and 95% expressed support for Mindset4Dementia in assessing another condition such as mental health.

Table 1. Characteristics of user population

Age	49.6 ± 17	(4,605)
Family history of dementia	40.4%	(1861)
Feeling significantly more forgetful	32.9%	(1513)
History of falls or feeling dizzy in the past year	37.0%	(709)
History of smoking or vaping	43.5%	(2002)
History of previous or current alcohol use	20.3%	(690)
History of diagnosed neurological condition	7.7%	(355)

Proportions and sample sizes of affirmative responses to questions from the targeted history section of Mindset4Dementia. This shows an adequate recruitment of the target population and a willingness to disclose information to the application.

Conclusion: This trial indicates successful design of an app that is highly user friendly in a representative age group for early detection of cognitive impairment. The next steps for Mindset4Dementia are to complete a formal clinical evaluation and apply for appropriate regulatory approval.

Disclosure: Authors were able to complete this work with the support of Mindset Technologies, Ltd., a privately held company.

EPR-253

Magnetic Resonance Spectroscopy Demonstrates Elevated Glutamate In Medically Unwell Older People With Delirium

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Background and aims: Delirium is an acute disorder of consciousness characterised by fluctuating consciousness and cognitive and physical dysfunction. It is common in medically unwell older people and is associated with significant morbidity and mortality. Accelerated cognitive decline following an episode of delirium suggests brain injury that is independent from other neurodegenerative processes. To investigate whether glutamate excitotoxicity may precipitate this injury. We quantified brain glutamate levels in medically unwell older people with delirium using 1-H Magnetic Resonance Spectroscopy.
Methods: Patients over 65 years old with and without delirium were recruited from medical wards at a single centre. Delirium severity was assessed alongside physical illness severity, frailty and prior cognitive decline. Structural and spectroscopy data was acquired in four prespecified brain regions. Peaks for glutamate + glutamine were normalised to that for total creatine (Glx/tCr) as a standard measure of brain glutamate concentration.
Results: Data was obtained from 10 delirium patients and five controls. Glutamate/tCr levels in parietal white matter were 14% higher on averaged in delirium compared to control patients (p=0.011). Exploratory analyses suggest that glutamate rather than glutamate was responsible for this difference. Additionally, we observed a positive correlation between the myo-inositol to tCr ratio (Ins/tCr) and white matter hyperintensity (WMH) burden across all subjects. After excluding patients with the highest WMH burden, delirium was associated with reduced Ins/tCr in the anterior cingulate cortex (p=0.020).
Conclusion: These data suggest that delirium is associated with elevated brain glutamate and offer a potential new treatment target to reduce post-delirium cognitive decline.
Disclosure: The authors declare no conflict of interest.

Movement disorders 5

EPR-254

Spastic paraparesis and ataxia – a new mutation in CSF1R gene

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Background and aims: The CSF1R gene encodes the colony stimulating factor 1 receptor (CSF1R), a transmembrane tyrosine kinase receptor that, in CNS, is mainly found in neurons and microglia, regulating their proliferation and survival. Mutations in this gene are found in the adult-onset leukoencephalopathy with axonal spheroids and pigmented glia (ALSP).
Methods: Case report
Results: A 52-year-old healthy woman, with unremarkable family history, presented in 2018 complaining of progressive gait impairment. The neurologic exam revealed pyramidal signs in all four limbs, appendicular ataxia and spastic gait. Brain MRI revealed bilateral hyperintense foci in FLAIR involving frontal and parietal white matter; spinal cord MRI was normal. Blood and CSF analysis and EMG showed no abnormalities. Once excluded acquired aetiologies, genetic panel for hereditary spastic paraplegias was requested and it was negative. Finally, a next generation sequencing panel for ataxias revealed a new mutation, in heterozygosity, in the CSF1R gene (c.730-3C>T); since it affects the splicing site, bioinformatic analysis predicts that this variant can be pathogenic. The neuroimaging remains stable, but clinically appendicular ataxia and lower limb spasticity is becoming progressively more severe.
Conclusion: ALSP is an autosomal dominant disorder, but sporadic cases have often been described. It is usually a rapid progressive leukodystrophy, clinically characterized by marked neuropsychiatric symptoms. Some patients, especially young women, can present with a different phenotype with spastic paraparesis as the main presentation. White matter lesions can be initially quite subtle, patchy and slowly progressive, contributing to a late diagnosis or misdiagnosis.
Disclosure: Nothing to disclose.

EPR-255

The C-terminal crosslinked telopeptide of type I collagen (CTX-I) as a cardiomyopathy biomarker in Friedreich Ataxia

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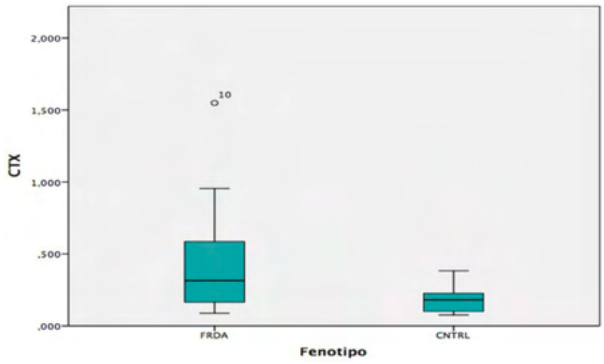
Background and aims: Friedreich ataxia (FRDA) is an autosomal recessive ataxia in which frataxin's reduction causes oxidative stress which interests not only CNS but also cardiac cells, causing Hypertrophic Cardiomyopathy (CM. In CM, extracellular matrix is predominantly composed of collagen type I. Its Cterminal crosslinked telopeptide (CTX-I) is released into blood. Our aim is to show if CTX-I can be considered an early biomarker able to predict CM in FRDA patients before it was clinically evident.
Methods: We measured serum CTX-I with ELISA technique in 24 FRDA patients and 19 healthy controls (HC). CTX-I levels were correlated to morphological cardiac changes established with Echocardiography; clinical features using the Scale for the Assessment and Rating of Ataxia (SARA) and biochemical markers.

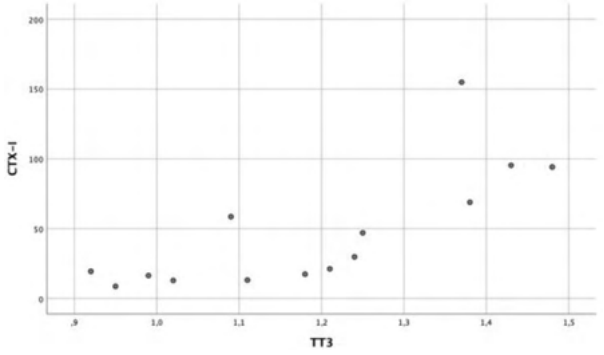
	HEART STATUS			
	Normal (n=6)	Concentric Remodelling (n=9)	Concentric Hypertrophy (n=4)	Eccentric Hypertrophy (n=1)
	Mean ± SD	Mean ± SD	Mean ± SD	Mean
IVS	9.1 ± 0,9	11,1 ± 2	12 ±1,4	13
PWTd	8,8 ± 0,8	9.9 ± 1	11.3 ± 1	10
PWTs	12 ± 1	16 ± 2	16 ± 3	.
LVEDD	46,2 ± 4,9	41.7 ± 2,6	45.7 ± 5,5	59
FS	23,4 ± 6,3	23,8 ± 10	28.6 ± 14	28.4
EF	0.542 ± 0,049	0.574 ± 0,081	0.639 ± 0,162	0.350
LVM	140,5 ± 41,9	141.6 ± 20,3	199.2 ± 52,7	288
EA	1,93 ± 0,63	1.31 ± 0,65	1.16 ± 0,56	.
RWT	0.381 ± 0,015	0.528 ± 0,165	0.490 ± 0,024	0.339

Cardiological Evaluation: Echocardiography (EcoCG): Four classes based on left ventricular mass index and relative wall thickness: elevated RWT with increased LVMI identified as concentric hypertrophy, elevated RWT with normal LVMI as concentric remodelin

Results: There wasn't statistically significant difference between FRDA and HC in demographic variables. CTX-I was inversely correlated with age (r=- 0,535; n=44; p<0.001), so we excluded patients under 18-year-old. Using a parametric unpaired student t test, we found a statistically significant difference in CTX levels between FRDA patients and HC even if Echocardiographical variables showed no differences between the groups. CTX-I Mean±SD were 43.8±38.6 g/L in FRDA and 18.2±8.3 g/L in HC (+25.7 g/L; CI +6.1, +45.2; p=0.007). Bivariate correlation analysis found a correlation between CTX-I value and TT3 (CM biomarker) (r=0.833; p<0.001).



The Shapiro-Wilk analysis highlighted a non-Gaussian distribution of CTX-I values ($p<0.001$). Normalization using a natural logarithm obtained a significantly better distribution ($p=0.56$) so that a parametric unpaired student t test could be used. CTX



Bivariate correlation analysis found a correlation between CTX-I value and TT3 ($r=0.833$; $p<0.001$).

Conclusion: We report a higher CTX-I levels in FRDA patients compared to HC. Its relationship with TT3 and echocardiographical variables makes it a new available marker useful to predict and prevent CM in FRDA.
Disclosure: Fredreich Ataxia, Hypertrophic Cardiomyopathy, early diagnosis, prognostic marker

EPR-256

Axial Posture Disorders and Their Clinical Correlates in Parkinson´s disease

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Background and aims: Postural disorders are frequently observed in Parkinson's disease (PD) and may cause disability. Although rigidity, dystonia, myopathy, proprioceptive disorders like conditions are discussed in their pathophysiology, the mechanism is not fully elucidated. In addition,the majority of these patients have no response to common treatments. These conditions need to be better understood in order to develop more effective treatments. The aim of this study is to describe the axial posture disorders observed in our PD patients and their associated clinical features.
Methods: In this single center study, PD patient records were reviewed.The frequencies of postural disorders were determined, and the demographic and clinical characteristics of the patients with and without postural disorders were compared.
Results: 127 idiopathic PD patients records were screened. Axial posture disorder was found in 55 patients (42,6%). Anteflexion was detected in 34,9% and camptocormia in 6,2% of PD patients. Patients with axial posture disorders were older at follow up and at disease oncet and also had longer disease duration. Additionally mean levodopa dose was higher in the postur disorder group. Initial symptome was bradikinesia in 78,2% of patients with posture disorder. H-Y score significantly higher in posture disorder group. Moreover, postural instability and falls were significantly common in the patients with axial posture disorders.
Conclusion: Posture disorder was observed in nearly half of the patients. Posture disorders are observed more frequently in patients with more advanced disease. This leads us to review the factors involved in disease progression in postural disorders pathogenesis. In addition, it is important to follow up patients who present with bradykinesia, which is more risky for developing postural disorders.
Disclosure: Nothing to disclose.

EPR-257

Application of the "5-2-1" Screening Criteria in Advanced Parkinson's disease Patients: Analysis from the COSMOS Study

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Background and aims: The 5-2-1 criteria developed by a Delphi expert consensus panel proposed that fulfilling at least one of the following would suggest advanced Parkinson's disease (APD): five times oral levodopa taken/ day, Two hours of OFF time/day, or one hour/day of troublesome dyskinesia (TSD). These criteria aid in the identification of patients inadequately controlled on oral/ transdermal medication, and may benefit from treatment modifications, including levodopa-carbidopa intestinal gel (LCIG).

Methods: COSMOS (COmedication Study assessing Mono- and cOmbination therapy with levodopa-carbidopa inteStinal gel) is a multi-country, cross-sectional and retrospective observational study enrolling APD patients treated with LCIG for 12 months (NCT03362879). This post-hoc analysis grouped patients based on fulfillment of one or more of the 5-2-1 criteria (Table 1). Assessments included patient demographics, disease characteristics, and motor complications.

Results: All patients fulfilled one criterion at baseline. The clinical profile showed additional deterioration as the number of criteria met increased (Table 2). All groups had improvement in OFF time with a mean difference of -4.4/ -3.9/ -4.2 hours for 1/ 2/ and 3/ criteria, respectively. Patients meeting two criteria had a significant reduction in severity of dyskinesia, tremor, freezing of gait and gait impairment from baseline ($p<0.0001$) with LCIG treatment. Patients meeting all criteria demonstrated reduction in severity of rigidity and nocturnal/morning akinesia from baseline ($p<0.0001$) with LCIG. Safety events were in line with the known LCIG profile.

Table 1. COSMOS Patients Who Met One or More of the 5-2-1 Criteria for APD

Number of Criteria Fulfilled	N (%)
1	51 (19.3)
2	152 (57.6)
3	61 (23.1)
Criteria Fulfilled	**N (%)**
≥1 hour/day of troublesome dyskinesia	6 (2.3)
≥2 hours of OFF time/day	45 (17)
≥5 times oral levodopa taken/day	0 (0)
≥2 hours of OFF time/day and ≥1 hour/day of troublesome dyskinesia	132 (49.8)
≥1 hour/day of troublesome dyskinesia and ≥5 times oral levodopa taken/day	3 (1.1)
≥5 times oral levodopa taken/day and is ≥2 hours of OFF time/day	17 (6.4)
All 5-2-1 criteria	61 (23)

COSMOS = COmedication Study assessing Mono- and cOmbination therapy with levodopa-carbidopa inteStinal gel. APD= Advanced Parkinson's disease.

Table 1. COSMOS Patients Who Met One or More of the 5-2-1 Criteria

Table 2. Baseline Demographics and Disease Characteristics

	Number of criteria fulfilled		
Characteristic	**1 N=51**	**2 N=152**	**3 N=61**
Gender			
Male	38 (74.5%)	37 (60.7%)	42 (68.9%)
Patients on LCIG Monotherapy*	19 (43.2%)	48 (32.7%)	20 (32.8%)
		mean ± SD	
Age at LCIG initiation, years	65.6± 10.1[a]	66.3 ± 7.7	65.6 ± 8.2
Time from PD diagnosis to LCIG initiation, years	11.6 ± 5.5[a]	12.7 ± 5.6[b]	13.1 ± 4.4
Time from PD diagnosis to dyskinesia, years	7.8 ± 3.4[c]	8.3 ± 4.4[d]	8.5 ± 3.2[e]
Time from PD diagnosis to wearing off, years**	6.7 ± 3.3[f]	7.0 ± 3.9[g]	8.1 ± 3.2[h]
Duration of LCIG treatment, months	34.7 ± 24.3	32.0 ± 18.9	36.0 ± 21.9
Duration of "Off" state during 24h', hours	6.6 ± 4.8	5.9 ± 3.2	6.1 ± 3.1
Duration of dyskinesia state during 24h, hours **	0.6 ± 1.9	4.1± 3.1	5.2 ± 2.6

*LCIG Monotherapy was defined as LCIG being the only PD therapy provided to the patients. ** $p<0.0001$ observed between groups. [a] n=48, [b] n=47, [c] n=20, [d] n= 134, [e] n= 60, [f] n=42, [g] n=143, [h] n= 58. 'Duration of "OFF" state and dyskinesia were calculated using the UPDRS Part IV items 32 and 39. LCIG = levodopa-carbidopa intestinal gel; PD = Parkinson's disease; SD = standard deviation.

Table 2. Baseline Demographics and Disease Characteristics

Conclusion: Patients fulfilling more of the 5-2-1 criteria had greater disease burden. Patients treated with LCIG meeting one criteria had improved OFF time, and other motor symptoms.

Disclosure: This study was funded by AbbVie Inc. AbbVie Inc. participated in the study design, study research, collection, analysis, and interpretation of data; and writing, reviewing, and approving this abstract for submission.

EPR-258

Potential protective role of ACE-inhibitors and AT1 receptor blockers against levodopa-induced dyskinesias

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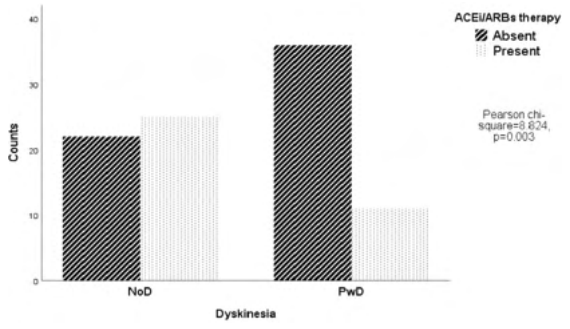
Background and aims: ACE-inhibitors (ACEi)/AT1 receptor blockers (ARBs) may influence the interplay between dopamine and the renin-angiotensin system in the nigrostriatal pathway, thus playing a role in the development of levodopa-induced dyskinesia in Parkinson's disease (PD).
Methods: We conducted a retrospective case-control study identifying PD patients with dyskinesias (PwD), n=47. Motor symptoms and disease staging were assessed using the UPDRS part III-IV and the HY scale. Non-dyskinetic controls (NoD) were nearly perfectly matched with a 1:1 ratio according to sex, UPDRS-III score (±2 points), and duration of antiparkinsonian treatment (±2 years). The difference in distribution between groups was analyzed through the two test or Fisher's exact test, whereas binary logistic regression was used to evaluate the association between dyskinesias and ACEi/ARBs use.
Results: 94 PD patients were included, aged 72.18±9 years, with an average disease duration of 10.20±4.8 years and 9.04±4.9 years of antiparkinsonian treatment. The mean UPDRS-III score was 18.87±7.6 and the median HY stage was 2. In the NoD group, 25 (53.2%) were users, and 22 (46.8%) non-users of ACEi/ARBs. Conversely, in the PwD group, 11 (23.4%) were users and 36 non-users (76.6%) of this drug class (Pearson chi-square=8.824, p=0.003). After controlling for remaining confounding predictors (tremor dominant phenotype, LEDD, HY 3-4, and disease duration), ACEi/ARBs use was a significant predictor of a lower occurrence of dyskinesia (OR=0.226; 95% CI 0.080–0.636; p=0.005).



ACEi/ARBs therapy in patients with (PwD) and without (NoD) dyskinesia

Conclusion: Our findings suggest a possible role of ACEi/ARBs in reducing dyskinesia among PD patients. Further studies with prospective, randomized, and controlled designs are warranted to confirm our preliminary results.
Disclosure: Nothing to disclose.

EPR-259

Mutations in the codon- 1441 of LRRK2 gene and Parkinson's disease in Russia

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Background and aims: Parkinson's disease (PD) is the second most common neurodegenerative disorder after Alzheimer's disease. Mutations in the leucine-rich repeat kinase 2 gene (LRRK2) are a common cause of familial and sporadic PD. To date, seven pathogenic mutations (N1437H, R1441C/G/H, Y1699C, G2019S, I2020T) in this gene have been described. The aim of our study was to assess the frequency of mutations in codon-1441 of the LRRK2 gene among PD patients and controls in North-Western region of Russia.
Methods: We screened 1,050 patients (mean age: 64.92±10.73) with PD and 500 ethnically matched controls subjects (mean age: 65.22±11.79) without neurological disorders from the North-Western region of Russia. Mutations in codon-1441 of LRRK2 gene were genotyped using PCR with the following restriction analysis. All found mutations were verified by direct sequencing of PCR products.
Results: The R1441C (c.4321C>T) mutation was revealed in two patients with sporadic form of PD (2/1050, 0.2%). A synonymous variant R1441R (c.4323C>T) that abolishes the restriction site for the endonuclease Bsh1236I was found in another two sporadic PD patients (2/1050, 0.2%). All found genetic variants were identified in heterozygous state and were not detected in controls.
Conclusion: The R1441C (c.4321C>T) mutation was revealed in two patients with sporadic form of PD (2/1050, 0.2%). A synonymous variant R1441R (c.4323C>T) that abolishes the restriction site for the endonuclease Bsh1236I was found in another two sporadic PD patients (2/1050, 0.2%). All found genetic variants were identified in heterozygous state and were not detected in controls. This research has been supported by RFBR grant 18-015-00262.
Disclosure: The author have Nothing to disclose.

EPR-260

Influence of onset of motor fluctuations in the Opicapone effectiveness in Parkinson's: real-world OPTIPARK study

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Background and aims: Opicapone (OPC) proved to be effective in treating end-of-dose motor fluctuations (MF) in Parkinson's disease (PD) patients [1,2]. The OPTIPARK study evaluated OPC 50mg in a heterogeneous population of patients treated in real-world conditions [3].

Methods: OPTIPARK was a prospective, open-label, single-arm trial conducted in Germany and the UK. Patients with MF received OPC 50mg in addition to current antiparkinsonian treatment. Primary efficacy 3-month endpoint was Clinician's-Global-Impression-of-Change (CGI-C). Secondary efficacy endpoints included Patient's-CGI-C (PGI-C), 8-item PD-Questionnaire (PDQ-8), Unified PD Rating Scale (UPDRS) and Non-Motor Symptoms Scale (NMSS). Safety assessments included evaluation of treatment-emergent adverse events (TEAEs). This post-hoc analysis evaluated the influence of onset MF (OMF) at baseline in patients who completed the study for each outcome.

Results: 393 (82.4%) patients completed the 3-month endpoint (completers-set, Table 1). Of these, although somehow similar, patients with higher OMF reported greater improvements' perception on CGI-C and PGI-C, when compared to recent fluctuators' patients (1year OMF) (Table 2). Still, recent fluctuators experienced greater improvements on UPDRS-II, quality-of-life (PDQ-8) and non-motor symptoms (NMSS) – no difference was observed for UPDRS-III – (Table 3). Furthermore, lower incidence of TEAEs considered at least possibly related to OPC were also reported for recent fluctuators (Table 3).

Table 1. Baseline characteristics (Completer-Set)

Category	≤ 1year of OMF N=177	> 1 year of OMF N=216
Age, mean (SD)	67.8 (9.5)	66.7 (8.7)
Male, n (%)	110 (62.1)	147 (68.1)
PD duration, mean (SD) years	6.6 (4.0)	9.8 (4.6)
Onset of MF, mean (SD) years	0.4 (0.3)	4.0 (3.2)
L-dopa amount, mean (SD) mg	501 (209)	604 (265)

SD, standard deviation; PD, Parkinson's Disease; MF, motor fluctuations; OMF, onset of MF

Table 2. CGI-C and PGI-C results after 3 months (Completer-Set)

Category	≤ 1year of OMF N=177 n (%)	> 1 year of OMF N=216 n (%)
CGI-C		
Not assessed	-	-
Very much improved	10 (5.6)	20 (9.3)
Much improved	67 (37.9)	100 (46.3)
Minimally improved	61 (34.5)	62 (28.7)
No change	32 (18.1)	24 (11.1)
Minimally worse	6 (3.4)	7 (3.2)
Much worse	-	3 (1.4)
Very much worse	1 (0.6)	-
PGI-C		
Not assessed	-	-
Very much improved	11 (6.2)	19 (8.8)
Much improved	69 (39.0)	90 (41.7)
Minimally improved	51 (28.8)	62 (28.7)
No change	30 (16.9)	28 (13.0)
Minimally worse	14 (7.9)	11 (5.1)
Much worse	1 (0.6)	5 (2.3)
Very much worse	1 (0.6)	1 (0.5)

OMF, onset of motor fluctuations; CGI-C, Clinician's Global Impression of Change; PGI-C, Patient's Global Impression of Change

Table 3. Secondary, after 3 months, and safety outcomes (Completer-Set)

Category	≤ 1year of OMF N=177 mean (SD)	> 1 year of OMF N=216 mean (SD)
UPDRS II (at ON stage)	-1.7 (3.8)	-1.6 (3.7)
p-value	*<.0001*	*<.0001*
UPDRS III	-4.6 (6.9)	-4.7 (9.0)
p-value	*<.0001*	*<.0001*
PDQ-8	-4.2 (13.3)	-2.8 (12.5)
p-value	*<.0001*	*0.0011*
NMSS	-7.7 (18.8)	-6.1 (20.5)
p-value	*<.0001*	*<.0001*
Any TEAE, **n (%)**	117 (66.1)	164 (75.9)
At least possibly related* TEAEs, **n (%)**	62 (35.0)	92 (42.6)

OMF, onset of motor fluctuations; SD, standard deviation; UPDRS, Unified Parkinson's Disease Rating Scale; PDQ-8, 8-item Parkinson's Disease Questionnaire; NMSS, Non-Motor Symptoms Scale; p-values obtained through Student's t-test for the change from baseline; *relationship to study medication reported as 'possible', 'probable', 'definite' or missing; TEAE, treatment-emergent adverse event (with onset or worsening after first opicapone intake until study termination, either regularly or prematurely)

Conclusion: Overall, these findings indicate that recent fluctuators may benefit, if not more, as much as patients with higher OMF from using OPC 50 mg as adjunctive therapy to levodopa.

Disclosure: 1.Ferreira et al., Lancet Neurology 2016;15 (2):154-165; 2.Lees et al., JAMA Neurol. 2017;74(2):197-206; 3.Reichmann et al., Transl Neurodegener. 2020;9(1):9

EPR-261

Effectiveness of Opicapone in Parkinson's according to baseline use of entacapone: the real-world OPTIPARK study

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Background and aims: Opicapone (OPC) proved to be effective in treating end-of-dose motor fluctuations (MF) in Parkinson's disease (PD) patients [1,2]. The OPTIPARK study evaluated OPC 50mg in a heterogeneous population of patients treated in real-world conditions [3].

Methods: OPTIPARK was a prospective, open-label, single-arm trial conducted in Germany and the UK. Patients with MF received OPC 50mg in addition to current antiparkinsonian treatment. Primary efficacy 3-month endpoint was Clinician's-Global-Impression-of-Change (CGI-C). Secondary efficacy endpoints included Patient's-CGI-C (PGI-C), 8-item PD-Questionnaire (PDQ-8), Unified PD Rating Scale (UPDRS) and Non-Motor Symptoms Scale (NMSS). Safety assessments included evaluation of treatment-emergent adverse events (TEAEs). This post-hoc analysis evaluated, for each outcome, the influence according to baseline use of entacapone (ENT) in patients who completed the study.

Results: 393 (82.4%) patients completed the 3-month endpoint (completers-set, Table 1). Of these, patients NOT using ENT at baseline experienced greater improvements on CGI-C and PGI-C, UPDRS-II and III, quality-of-life (PDQ-8) and non-motor symptoms (NMSS), when compared to patients using ENT (and switched) at baseline (Table 2, Table 3). Similar incidence of TEAEs considered at least possibly related to OPC were reported for both subgroups (Table 3).

Table 1. Baseline characteristics (Completer-Set)

Category	Used ENT at Baseline	Not Used ENT at Baseline
	N=126	N=267
Age, mean (SD)	65.5 (9.1)	68.0 (9.0)
Male, n (%)	84 (66.7)	173 (64.8)
PD duration, mean (SD) years	9.2 (4.2)	8.0 (4.8)
Onset of MF, mean (SD) years	3.0 (3.0)	2.1 (3.0)
Ldopa amount, mean (SD) mg	620 (239)	528 (246)

SD, standard deviation; PD, Parkinson's Disease; MF, motor fluctuations; ENT, entacapone

Table 2. CGI-C and PGI-C results after 3 months (Completer-Set)

Category	Used ENT at Baseline	Not Used ENT at Baseline
	N=126 n (%)	N=267 n (%)
CGI-C		
Not assessed	-	-
Very much improved	8 (6.3)	22 (8.2)
Much improved	45 (35.7)	122 (45.7)
Minimally improved	46 (36.5)	77 (28.8)
No change	19 (15.1)	37 (13.9)
Minimally worse	6 (4.8)	7 (2.6)
Much worse	1 (0.8)	2 (0.7)
Very much worse	1 (0.8)	-
PGI-C		
Not assessed	-	-
Very much improved	5 (4.0)	25 (9.4)
Much improved	47 (37.3)	112 (41.9)
Minimally improved	41 (32.5)	72 (27.0)
No change	19 (15.1)	39 (14.6)
Minimally worse	9 (7.1)	16 (6.0)
Much worse	4 (3.2)	2 (0.7)
Very much worse	1 (0.8)	1 (0.4)

ENT, entacapone; CGI-C, Clinician's Global Impression of Change; PGI-C, Patient's Global Impression of Change

Table 3. Secondary, after 3 months, and safety outcomes (Completer-Set)

Category	Used ENT at Baseline	Not Used ENT at Baseline
	N=126	N=267
UPDRS II (at ON stage), mean (SD)	-1.2 (3.5)	-1.8 (3.9)
p-value	*0.0001*	*<.0001*
UPDRS III, mean (SD)	-4.4 (7.9)	-4.8 (8.2)
p-value	*<.0001*	*<.0001*
PDQ-8, mean (SD)	-1.3 (13.6)	-4.5 (12.4)
p-value	*0.2953*	*<.0001*
NMSS, mean (SD)	-5.5 (23.8)	-7.4 (17.6)
p-value	*0.0099*	*<.0001*
Any TEAE, n (%)	99 (78.6)	182 (68.2)
At least possibly related[a] TEAEs, n (%)	49 (38.9)	105 (39.3)

ENT, entacapone; SD, standard deviation; UPDRS, Unified Parkinson's Disease Rating Scale; PDQ-8, 8-item Parkinson's Disease Questionnaire; NMSS, Non-Motor Symptoms Scale; p-values obtained through Student's t-test for the change from baseline; [a]relationship to study medication reported as 'possible', 'probable', 'definite' or missing; TEAE, treatment-emergent adverse event (with onset or worsening after first opicapone intake until study termination, either regularly or prematurely)

Conclusion: Overall, these findings indicate that patients not using ENT at baseline (representative of recent fluctuators) may have an added benefit from using OPC 50 mg as adjunctive therapy to levodopa.

Disclosure: 1.Ferreira et al., Lancet Neurology 2016;15 (2):154-165; 2.Lees et al., JAMA Neurol. 2017;74(2):197-206; 3.Reichmann et al., Transl Neurodegener. 2020;9(1):9

MS and related disorders 5

EPR-262

Impact of autologous haematopoietic stem cell transplantation on fertility in aggressive multiple sclerosis

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Background and aims: Autologous haematopoietic stem cell transplantation (AHSCT) is a treatment option for aggressive multiple sclerosis (aMS) with an acceptable safety profile, but few data are available so far on its impact on fertility.

Methods: Data on menses recovery following transplant and endocrine assessment (luteinizing hormone, follicle-stimulating hormone, oestradiol, progesterone, prolactin, testosterone, anti-müllerian hormone - AMH) were collected in aMS patients treated with AHSCT who had at least one endocrine assessment after transplant.

Results: 23 females and six males were included (table 1). After conditioning, 19/23 (83%) females experienced persistent amenorrhea. Four females showed spontaneous menses recovery within six months after transplant; these cases were younger compared to those who did not: median age at AHSCT 26 (range 24–39) vs 38 years (26–50), p=0.027. AMH was aligned with values expected according to patients' age in 8/9 evaluable cases (89%) at baseline, while at month six it decreased to levels below normal values in 7/9 cases (78%); a further reduction at month 24 was observed in 6/7 (86%) cases. Post-transplant AMH was normal in 2/14 (14%) females for whom only post-treatment assessment was available. No pregnancies were reported. In males, post-AHSCT testosterone levels were within the normal range in 5/6 cases and were not reduced compared to baseline in 2/3 (67%) evaluable cases.

	Females, n=23		Males, n=6	
	n	(%)	n	(%)
MS form, relapsing-remitting	17	(74%)	3	(50%)
MS form, secondary-progressive	6	(25%)	3	(50%)
Conditioning regimen, BEAM+ATG	21	(91%)	6	(100%)
Conditioning regimen, carmustine/etoposide/cytarabine or cyclophosphamide 200 mg/Kg+ATG	2	(9%)	0	(0%)
	median	(range)	median	(range)
Age at AHSCT, y	36	(24 – 50)	37	(20 – 53)
Disease duration from onset, y	11	(4 – 29)	8.5	(3 – 24)
Baseline EDSS	4.5	(1.5 – 6.5)	5.75	(2.5 – 6.5)
Treatment duration at AHSCT, y	8	(3 – 21)	7.5	(2 – 22)
Previous DMTs received, n	3	(2 – 7)	2.5	(2 – 5)
Previous exposure to DMTs	N (%)	Duration, m	N (%)	Duration, m
Alemtuzumab	1 (4%)	24	0	
Azathioprine	5 (22%)	56 (12 – 116)	1 (17%)	120
Copaxone	7 (30%)	17 (2 – 35)	2 (33%)	14, 94
Cyclophosphamide	13 (56%)	5 (2 – 22)	3 (50%)	1, 24, 3
Daclizumab	1 (4%)	48	0	
Dimethyl-fumarate	2 (9%)	1, 23	2 (33%)	6, 28
Fingolimod	9 (39%)	19 (4 – 64)	2 (33%)	1, 36
Interferons	18 (78%)	38 (4 – 206)	6 (100%)	39 (6 – 60)
Mitoxantrone	2 (9%)	3, 5	0	
Natalizumab	17 (74%)	24 (6 – 46)	3 (50%)	2, 24, 24
Rituximab	4 (17%)	6, 6, 6, 60	1 (17%)	18

Duration of treatment is reported as single values up to 4 cases, as median (range) for DMTs received by at least 5 cases.

Table 1: Baseline characteristics of the patients included in the study

Conclusion: Although exploratory, our data confirm that AHSCT deeply affects gonadal function in females, with the deepest effect in older women; a potential additive effect of prior immunosuppressive treatments cannot be ruled out. Gonadal function in males seems to be only minimally affected.

Disclosure: Nothing to disclose.

EPR-263

Cortical thinning and serum neurofilament light levels as predictors of cognition in Multiple Sclerosis patients.

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Background and aims: To assess if, in early diagnosed MS patients, the combination of MRI/blood neurodegeneration markers and neuropsychiatric scores may increase predictive value about cognitive performance and fatigue.
Methods: 35 early diagnosed relapsing-remitting MS patients and 23 healthy controls (HC) underwent neuropsychological assessment, structural brain MRI exploration, and serum neurofilament light (sNfL) levels testing. Two sample t-test were performed in order to assess differences between groups and stepwise multiple regression analyses were carried in MS group to determine if gray matter (GM) brain volumes, cortical thickness (CT), sNfL levels and neuropsychiatric scores may predict cognitive and fatigue scores.
Results: Compared to HC, MS patients exhibit lower performance in several cognitive functions and higher scores in depression, anxiety and fatigue tests. In addition, MS group also showed bilateral thalamic GM atrophy and a reduced CT in right superior temporal gyrus (STG) and transverse temporal gyrus (TTG). Regression analyses showed that, although there were no reliable predictors of fatigue scores, anxiety levels, sNfL levels and global CT were significant predictor of cognitive performance in MS patients. More specifically, regional CT of right TTG explained greater variance than global CT regarding cognitive performance.
Conclusion: GM thalamic atrophy and reduced temporal CT represent an early MRI surrogate in MS disease course. While sNfL levels considered in isolation do not appear to be an important feature in newly MS patients, its combination with CT measures could increase effectiveness as cognitive status predictors.
Disclosure: This project was funded by Spanish (RTI2018-096951-A-I00, ITI; PI-0025-2017, RYC-2015-18467) grants.

EPR-264

Demyelination and age influence neurodegeneration after acute optic neuritis

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Background and aims: Visual evoked potentials (VEPs) and optical coherence tomography (OCT) are used to monitor acute optic neuritis (aON), assessing demyelination and neurodegeneration. We applied these techniques to describe functional and structural damage after aON in relapsing-remitting multiple sclerosis (RRMS) or clinically isolated syndrome (CIS)..
Methods: Prospective longitudinal study enrolling 40 patients (16 CIS, 24 RRMS) with a first aON episode in the study eye, who underwent OCT and VEPs within four weeks after onset, with follow-up repeated at 3, six and nine months. Twenty-one patients also had acute phase data available.
Results: VEPs latency progressively recovered (mean change month 1–9: -8.5ms, $p<0.001$) with a parallel thinning of peripapillary retinal nerve fiber layer (pRNFL; -9.8µm, $p<0.001$); ganglion cells-inner plexiform layer (GCIPL) thinning already occurred within one month (n.21, -4.56µm, $p<0.001$). Using linear regression, pre-baseline VEPs latency (n.21, Adj.R2=0.153, -0.445, p=0.049) and GCIPL thinning over the 1st month (n.21, Adj.R2=0.647, 0.815, $p<0.001$) predicted subsequent pRNFL loss. Furthermore, VEPs latency >140ms at one month was significantly associated with pRNFL loss >5µm (2 5.79, p=0.016). In patients with VEPs latency <140ms at one month, age 33 years was associated with the same outcome (2 3.309, p=0.049).
Conclusion: Retinal damage is already evident one month after aON, particularly in patients with older age and with more severe early demyelination, as from VEPs latency. Hyperacute recruitment is crucial to prompt remyelinating and neuroprotective strategies.
Disclosure: Part of this work was supported by Merck, Geneva, Switzerland. Merck is the biopharmaceutical division of Merck KGaA, Darmstadt, Germany.

EPR-265

Atrophy of the posterior cerebellar lobules is related to episodic memory difficulties in multiple sclerosis

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Background and aims: Cerebellar pathology is associated with worse cognitive performances in patients with multiple sclerosis (MS), but the structural correlates of cognitive domains, mood disturbances and fatigue are still unknown.
Methods: Patients underwent 3T brain MRI (Siemens,Prisma) and neuropsychological evaluation with assessment of the symbol digit modalities test (SDMT), the California verbal learning test (CVLT) and the Brief visuospatial memory test (BVMT). They performed Hospital anxiety and depression scale (HADS) and modified fatigue impact scale (MFIS).
Results: We included 70pts [58(82.9%) with relapsing-remitting MS]; 52 females (74.3%), mean age 42.9 (±11.1) years] with a median baseline EDSS of 2.5 (1–7). Mean SDMT score was 54.3 (±13.7), mean CVLT score was 57.9 (±11.5) and mean BVMT score was 28.4 (±6.5). Mean HADS-a was 6.36 (±3.84), mean HADS-d was 5.08 (±3.74). HADS for anxiety and depression was not available in 2pts. 49pts performed MFIS with a mean score of 26,14 (±19.9). Mean cerebellar T1LV and cerebellar T2LV were 0.2 (±0.3) and 0.3 (±0.5). Correlations were found between volumes of the posterior lobe of the cerebellum, lobule VIIIa, VIIIb, IX and X and CVLT scores ($0.24<r<0.29$, $0.015<p<0.046$). Normalized Grey Matter was associated with SDMT score ($r=0.26$, $p=0.032$). No correlations were found between volume of posterior lobe of the cerebellum and measures of mood disturbances.
Conclusion: Atrophy of the cerebellar lobules VIIIa, VIIIb, IX and X is independently associated with episodic memory difficulties but not with increased anxiety and depression in MS patients, while processing speed seems to relate mostly to brain pathology.
Disclosure: MI received grants from the National Institutes of Health, National Multiple Sclerosis Society, and FISM and received fees for consultation from Roche, Genzyme, Merck, Biogen, and Novartis.

EPR-266

Retrospective in silico analysis of routine laboratory data corroborates unique association of Epstein-Barr virus and MS

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Background and aims: Retrospective in silico analysis of routine laboratory data (RISAROLDA) is a digital approach for investigating laboratory parameters in large numbers of patients. We applied this approach to study the association of Epstein-Barr virus (EBV) and multiple sclerosis (MS).
Methods: We conducted RISAROLDA in 9,519 patients with an ICD10 diagnosis of MS treated at Charité–Universitätsmedizin Berlin between 2000 and 2020. 32,510 patients with ICD10 diagnoses of seven further inflammatory/neoplastic diseases were included as controls. Results of serologies and determinations of antibody indices (AI) for EBV, measles, mumps, rubella, herpes simplex (HSV) and varicella zoster virus (VZV) were collected from patients with MS. EBV serologies were likewise compiled from controls.
Results: 332/332 (100%) patients with MS with EBV serologies available were EBV seropositive. EBV seropositivity of patients with sarcoidosis (157/164), arthritis (105/109), neuromyelitis optica (33/37), systemic lupus erythematosus (162/169), Sjogren's disease (102/104), Hodgkin's (343/375) and Burkitt's lymphoma (84/96) ranged from 87.5% to 98.1%. In patients with MS, seropositivity to measles (269/280, 96.1%), rubella (107/113, 94.7%), mumps (72/87, 82.8%), HSV (270/367, 73.6%) and VZV (518/529, 97.9%) was lower than that to EBV, but the frequency of elevated measles (263/488, 53.9%), mumps (41/133, 30.8%), rubella (233/451, 51.7%), HSV (115/360, 31%) and VZV (395/680, 58.1%) AIs was higher than that of an elevated EBV AI (31/151, 20.5%).
Conclusion: The 100% EBV seropositivity and the paradoxically low intrathecal EBV antibody production in patients with MS corroborates a unique association of EBV and MS. RISAROLDA is powerful tool for analysis of real world laboratory data.
Disclosure: KR received research support from Novartis, Merck Serono, German Ministry of Education and Research, European Union (821283-2), Stiftung Charité (BIH Clinical Fellow Program) and Arthur Arnstein Foundation.

EPR-267

Tapping Fatigability Index as a Proxy for Fatigue: An In-The-Wild mHealth Study in MS Patients

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Background and aims: Fatigue is not well understood despite being a highly prevalent and debilitating symptom in MS patients. While fatigue is a subjective symptom, fatigability can be measured objectively and is hence a promising approach to study fatigue in patients. Finding ubiquitous and inexpensive ways to assess fatigability could help to understand the symptom and develop objective outcome parameters for assessing novel therapies.
Methods: We conducted a 2-week in-the-wild study. We use the fatigue scale for motor and cognitive functions (FSMC) to discriminate between motor and non-motor-fatigued participants. As a motor fatigability task, we use the rapid alternating finger-tapping task on a smartphone. Through we evaluate our metrics' performance to rank fatigued vs. non-fatigued participants in relation to the FSMC. Our study population included a group of MS patients and healthy controls. Each participant performed the rapid alternating finger-tapping task with their dominant hand daily.
Results: In summary, our results show that: (1) our metric Tapping fatigability index can discriminate between fatigued and non-fatigued participants with A=0.75±5. (2) Tapping as a fatigability task is valid in unsupervised settings. (3) Tapping frequency can be used as a measurement of MS-related disability=0.89±6.
Conclusion: We introduced a new mobile-based metric as a proxy to objectively quantify motor fatigue. We believe that our work is the next step towards the ubiquitous and objective quantification of fatigue. This approach offers an advantage over traditional fatigue questionnaires by being less subjective to confounding factors.
Disclosure: Nothing to disclose.

EPR-268

Transnasal administration of anti-Nogo-A antibody alleviates the symptoms of experimental autoimmune encephalomyelitis

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Background and aims: The CSF administration of Nogo-A-neutralizing IgG can promote remyelination and axonal repair in experimental models of multiple sclerosis (MS) such as experimental autoimmune encephalomyelitis (EAE). However, the weak ability of IgG to cross the blood-brain barrier limits the development of antibody-based treatment for MS, when using the peripheral routes of administration such as intravenous injections. To circumvent this issue, we developed a transnasal approach allowing repeated and minimally-invasive applications of Nogo-A-blocking antibody (11C7).
Methods: Under isoflurane anaesthesia, a gel matrix containing 30ug of 11C7 or control IgG administered daily with a catheter-adapted Hamilton syringe onto the nasal mucosa of each nostril. EAE was induced with subcutaneous injection of recombinant myelin oligodendrocyte glycoprotein peptide (MOG35-55; 200ug). EAE symptoms were scored for 30 days as follows: 0.5 (limp tail), one (hindlimb weakness), two (hindlimb paraparesis), three (hindlimb paraparesis and incontinence). The spinal cord and brain of EAE mice were then collected for transcriptomic analysis and histological examination.
Results: Transnasal application of Nogo-A blocking mAb 11C7 improves the clinical symptoms of EAE mice after the peak of the disease (~day 20) compared with control IgG treatment ($p<0.001$). Transcriptomic results suggest that 11C7 influences gene expression in EAE brains relative to control IgG. Ongoing histological observations will allow to determine if the therapeutic effects of 11C7 are associated with remyelination in the spinal cord.
Conclusion: The nose-to-brain strategy may be a new efficient approach to alleviate the clinical symptoms of autoimmune diseases targeting myelin in the CNS.
Disclosure: This study is part of the Nose-to-Brain-patch project (N2B-patch), an EU-funded project of the H2020-EU.2.1.3. program (#721098)

EPR-269

Assessment of Composite Disability Accumulation of ponesimod relative to teriflunomide in the OPTIMUM Phase 3 study

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Background and aims: In relapsing forms of Multiple Sclerosis, disability progression has been shown to be independent of relapses. A new concept in MS research has emerged, PIRA or Progression Independent of Relapse Activity. Expanded Disability Status Scale (EDSS) is a widely used scale for assessing disability but relies excessively on lower body mobility, neglecting other aspects of disability progression. A composite of confirmed disability accumulation (CDA) including EDSS scores, 9-hole peg test, and timed 25-foot walk would be more comprehensive and sensitive assessment of disease progression.
Methods: Using results from the OPTIMUM study, time to 1st composite 12-week CDA was compared between ponesimod 20mg and teriflunomide 14mg. Additional analyses were conducted to assess PIRA. Hazard ratios and 95% confidence intervals were calculated to test the treatment effect between the two compounds.
Results: At week 108, composite CDA was reached during the study by 18.2% and 24.0% of subjects in the ponesimod 20mg and teriflunomide 14mg groups, respectively. The relative risk of an event was estimated to be 24% lower with ponesimod 20mg, with the difference being statistically significant at a significance level of 5% (hazard ratio: 0.76 95% CI = 0.59–0.98; p-value=0.0346). The sensitivity analyses for PIRA and non-relapsing subjects yielded similar results.
Conclusion: Using a more comprehensive measure of disability worsening, a statistically significant difference and clinically meaningful treatment effect of ponesimod versus teriflunomide was established. This treatment effect is also present when considering disability worsening independent of relapse activity.
Disclosure: Janssen R&D

Neuroimmunology

EPR-270

A Computational Model using Quantum Mechanics for Neuroimmunological Aspects Related to Tau Protein and Amyloid-Beta

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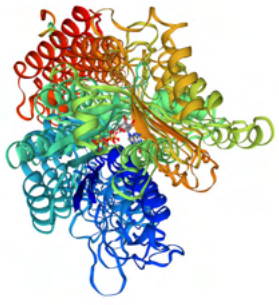
Background and aims: Protein aggregation is a common feature of neurodegenative diseases, along with other changes in the various cellular compartments. Specifically in Alzheimer's disease, aggregates are found containing the hyperphosphorylated Tau protein and the beta-amyloid peptide. This study aims to develop a computational model using quantum mechanics for neuroimmunological aspects related to the Tau protein and amyloid-beta peptide.
Methods: The molecular docking of Tau protein and amyloid-beta peptide were conducted with the tool AutoDock Vina (version 1.1.2), as implemented in the MolAr (Molecular Architecture) software. The loop regions were rebuilt using the Modeller. Key docking complexes were evaluated by molecular dynamics (MD) simulation using the GROMOS54A7 all-atom force field and performed using GROMACS 5.1 software. Using deterministic model based on Dirac notation, stochastic model using the stochastic differential equation with Poisson point process and Jackknife-Monte-Carlo Approach, a computational model was developed. Other software used in this work to neuroimmunology analysis were: ACD/ChemSketch, ABCpred, BepiPred-2.0, AxonDeepSeg, Computer-assisted Evaluation of Myelin formation, Visual Molecular Dynamics, C-ImmSim and Simmune.
Results: Amyloid-beta peptide presented, in computational model, a preferential interaction with the phosphorylation site R2 of Tau. It was identified that the hyperphosphorylation of the Tau protein seems to interfere in the binding of motor proteins favoring appearance of neuroinflammatory phenomena and presence of immune cells inducing immunomediated tissue damage. This work also identified association of miRNA (miR-132, miR-129) with neuritic -amyloid plaques and neurofibrillary tangle.
Conclusion: Understanding pathological mechanisms should help developing therapeutic tools to treat diseases with problems related to the tau protein and amyloid-beta peptide.
Disclosure: Nothing to disclose.



Model of synthetic tau (R2x4) bound to the microtubule

EPR-271

Diagnostic changes in inflammatory myelitis – a 12-year retrospective study

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Background and aims: Myelopathies diagnosis is challenging. An accurate etiology might be difficult to ascertain at the time of 1st hospital admission. We evaluated diagnostic changes in patients with inflammatory myelitis upon follow-up.
Methods: We included adult patients with a diagnosis of inflammatory myelitis, admitted to the Neurology ward of a tertiary hospital between 2007 and 2018. Patients had at least one year of follow-up. We evaluated sociodemographic characteristics, diagnosis at the time of discharge, final diagnosis after follow-up, and reason for the diagnostic change.
Results: 80 patients, with a median follow-up of 62.5 months (IQR 38–102), met study inclusion criteria: 49 (61.3%) were female, with a median age at symptom-onset of 29.5 years (IQR 24–46). Diagnosis at discharge were: 45% multiple sclerosis (MS), 35% idiopathic acute transverse myelitis (IATM), 1.3% post-infections myelitis, 12.5% neuromyelitis optica spectrum disorder, 3.8% acute disseminated encephalomyelitis, and 2.5% sarcoidosis. 23 patients (28.7%) changed diagnosis after a median of 18 months (IQR 10–25): 75% were initially classified as IATM and ultimately changed to clinically isolated syndrome (17.9%), MS (46.4%), NMOSD (7%), and Behçet's (3.6%). These had a younger age at symptom-onset (28 vs. 33, p=0.084), and a lower EDSS at admission (2.5 vs 3.5, p=0.042). Changes occurred due to clinical evolution (56.3%), imaging criteria (3.5%), and laboratory criteria (6.3%). Overall, patients who changed diagnosis had a longer time until relapse (10 months vs. six months, p=0.034).
Conclusion: Diagnostic changes are not infrequent in patients with IATM. These patients require appropriate follow-up time and dedicated clinical/paraclinical evaluation, increasing diagnostic accuracy.
Disclosure: No disclosures.. Leonor Dias and Leonardo Barbosa contributed equally to the present work.

EPR-272

Multiple sclerosis in pediatric age

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Background and aims: Pediatric-onset multiple sclerosis (POMS) represents between 3–10% of all MS diagnosis. In 2017, MS criteria were defined in adults and these criteria can be used in children above 11 years if the first attack is not ADEM.
Methods: To characterize the pediatric-onset MS cohort of a third level hospital. Retrospective observational study. Clinical records of all patients with multiple sclerosis onset younger than 18 years were revised between 2011 and 2020. Demographic, clinical, laboratorial, MRI and treatments were collected.
Results: We identified 21 patients with a distribution by gender 11M:10F. The average age of onset was 14.8 years (10-17). The initial clinical manifestations were: myelitis in 15 patients, supratentorial symptoms in 5, cerebellar syndrome in six and two had optic neuritis. Five had politopic presentation. 18 (85,7%) patients had CSF specific oligoclonal bands. Brain MRI showed supra and infratentorial involvement in 17 patients. Relapses were treated with intravenous steroids in 19 patients. 10 patients are on 1st line treatments (9-beta-interferon, 2-teriflunomide), 10 on 2nd line treatments (6-natalizumab, 3-fingolimod, 1-ocrelizumab) and one has not started yet. With an average of three years and 10 months of follow-up (2M-9Y) and a mean annualized rate of 0,29 (0,01–3). EDSS: 0 (7 patients); 1 (6); 1,5 (2); 2 (5); 3 (1); four have learning disability/memory changes; all cases have the relapsing-remitting course.
Conclusion: Prompting growing efforts to characterize the spectrum of pediatric onset MS are important because an earlier disease onset may impact cognitive and physical disability in adulthood.
Disclosure: N/A

EPR-273

The Role of a Tissue-based Assay in the Diagnosis of Autoimmune Encephalitis

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Background and aims: To evaluate the sensitivity and specificity of an indirect immunofluorescence (IIF) assay on a composite substrate of murine tissue sections (tissue-based assay, TBA) for the diagnosis of autoimmune encephalitis (AE).
Methods: Serum and cerebrospinal fluid (CSF) specimens of patients with suspected AE, collected from December 2012 and September 2020, were tested by an IIF-TBA. Clinical and demographic data were obtained by chart review.
Results: AE was diagnosed in 83/159 (52%) patients. IIF-TBA revealed an immunoglobulin G-specific immunoreactivity restricted to the nervous system in 82/159: 71 (87%) had AE, while in 11 (13%) other diseases were ascertained (9 herpes simplex virus encephalitis, one bacterial meningoencephalitis and one stroke). Among patients with AE, 12/83 patients (14%) tested negative by IIF-TBA. Serum testing showed 85.5% sensitivity and 90.2% specificity for the diagnosis of AE, whereas CSF testing had 61.9% sensitivity and 84.9% specificity. For 94/159 patients with available paired samples (both serum and CSF), serum showed higher sensitivity than CSF, while the latter had higher specificity.
Conclusion: IIF-TBA is a valuable screening method in patients with suspected AE; both serum and CSF testing are recommended. Microbiological investigations should never be dismissed, however, since a positive result does not rule out infectious diseases.
Disclosure: No disclosures. to report.

EPR-274

Pembrolizumab-induced myasthenic syndrome

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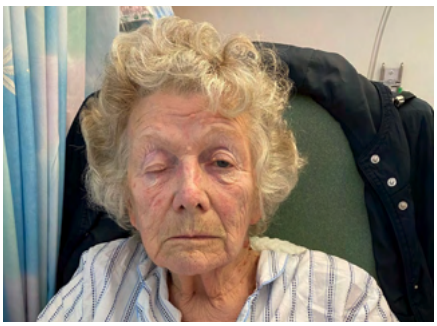
Background and aims: Pembrolizumab is a monoclonal antibody that inhibits programmed cell death 1 receptor (PD-1) and increases immune response to malignancy. By expressing PD-L1 (programmed cell death ligand 1), many cells, including neurons, are protected against autoimmunity. While immunotherapy has revolutionised cancer treatment, serious autoimmune adverse events have been described. We report a rare case of pembrolizumab-induced myasthenic syndrome.
Methods: A 75-year-old female presented with right-sided ptosis, generalised weakness, head drop, fatigue and slurred speech on a background of pembrolizumab treatment for metastatic melanoma. A clinical diagnosis of myasthenic syndrome secondary to immunotherapy was made and initial therapy was instituted in the form of prednisolone, pyridostigmine and IVIg. No improvement ensued and she subsequently underwent plasmapheresis. Unfortunately, the patient deteriorated with worsening respiratory function and passed away. Of note, her anti-acetylcholine receptor and anti-muscle specific kinase antibodies returned negative.



Right-sided ptosis post-pembrolizumab (consent for academic publication obtained from patient)

Results: The estimated prevalence of this complication is <1%. This syndrome can occur a median of four weeks after immunotherapy initiation. Respiratory failure occurs in half of cases and myositis occurs in approximately 40% of cases. Anti-acetylcholine receptor and anti-muscle specific kinase antibodies are negative in one-third. Better outcomes have been observed in patients who received IVIg/plasmapheresis as 1st-line therapy than in those who received steroids alone. The overall mortality rate is approximately 40%.
Conclusion: EPR-274 Pembrolizumab-induced myasthenic syndrome has a high mortality rate and can occur a median of four weeks after treatment. Consideration should be given prior to initiation of therapy about immunotherapy's rare, yet serious, side effects.
Disclosure: The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

EPR-275

Relapsing remitting encephalomyelitis with GAD antibodies following autologous haematopoietic stem cell transplantation

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Background and aims: Antibodies to glutamic acid decarboxylase (GAD) are related to several neurologic syndromes and have been rarely described following allogenic or autologous hematopoietic stem cell transplantation (aHSCT). Despite being used to treat refractory autoimmune disorders, new autoimmunity following aHSCT is an increasingly recognized phenomenon.
Methods: Case report
Results: 28-year-old male with acute promyelocytic leukaemia was submitted to aHSCT in 2012. 10 months later, he developed seizures and mental status disturbance. Brain MRI and EEG were highly suggestive of limbic encephalitis and GAD antibodies were positive in blood and CSF (>2,000U/mL). He was treated with steroids and immunoglobulin with good response. In 2014, he presented with diplopia and left facial palsy with a new pontine lesion on MRI, again positive for GAD antibodies in serum and CSF. This time he was kept on alternating cycles of immunoglobulin and plasmapheresis for one year with clinical and imaging improvement; however, his GAD antibodies remained positive. In 2016, a new spinal cord transverse lesion was identified and treatment with azathioprine was tried, but failed to maintain remission. Finally, he was treated with rituximab and, since then, he remains clinically stable with negative GAD antibodies. During these relapses an extensive investigation excluded infection, paraneoplastic or other autoimmune disorders.
Conclusion: To our knowledge this is the 1st case reporting anti-GAD immumediated encephalomyelitis following aHSCT. aHSCT aims to reconstitute the immune system to a self-tolerant state, however a combination of genetic predisposition, abnormal lymphopoiesis and tolerance imbalance can lead to a de novo autoimmune disorder.
Disclosure: Nothing to disclose.

EPR-276

Lowering plasma cholesterol does not affect neuroinflammation in a murine model of multiple sclerosis

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Background and aims: Multiple sclerosis (MS) is an inflammatory and autoimmune disease affecting the central nervous system leading to disabling neurological deficits. Environmental factors are important in MS development. In line with this concept, obesity and metabolic syndrome (MetS) are associated with increased MS risk. While the lipid-lowering drug statins could be beneficial in MS, few studies have examined the contribution of dyslipidemia and especially elevated cholesterol in this disease. Thus, whether circulating cholesterol should be targeted in MS remains debated.
Methods: We assessed the importance of circulating cholesterol using a MS murine model, the experimental autoimmune encephalomyelitis (EAE) and two different strategies: 1) a mouse model of familial hypercholesterolemia where genetic deletion of LDLr (coding for the low-density lipoprotein receptor) causes a significant increase of plasma cholesterol concentrations and 2) the use of a monoclonal PCSK9 inhibitor which reduces LDLr degradation and consequently lowers plasma cholesterol concentrations.
Results: We show that high plasma cholesterol concentrations induced by LDLr deficiency does not affect EAE independently of the mice sex. In addition, while a monoclonal PCSK9 inhibitor decreases cholesterol plasma concentrations, it does not influence EAE nor modulate the immune response in EAE.
Conclusion: These findings show that modulating circulating cholesterol does not affect the disease course of EAE and suggest that the protective effects of statins in MS are independant from circulating cholesterol. In the current knowledge, physicians and patients are advised to treat all MetS components in MS, instead of solely targeting circulating cholesterol with lipid-lowering drugs.
Disclosure: Caroline Pot has participated in advisory boards for Biogen, Celgene, Merck, Novartis and Roche none related to this work. The other authors have nothing to disclose.

EPR-277

Autoimmune encephalitis with antibodies against LGI1: broadening the spectrum of dystonic seizures.

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Background and aims: Facio-brachial dystonic seizures are the hallmark of antiLGI1 encephalitis. We present the cases of two women suffering cognitive impairment and dystonic seizures, involving the crural region in one and the cervical-brachial region in the other.

Methods: Description of two cases of anti-LGI1 encephalitis.

Results: Case 1. A 55-year-old woman presented progressive confusion and right cervical-brachial dystonic seizures. Brain MRI was unremarkable. V-EEG showed theta waves in the left temporal region, without correlation with the dystonic seizures. Treatment consisted on IVIG followed by rituximab. There was cognitive improvement and no new dystonic seizures after immunotherapy. Case 2. A 47-year-old woman with right crural dystonic seizures, up to 40 seizures per day who also complained about memory deficits and sleep disorder. Brain MRI was unremarkable at admission, but control brain MRI after six months showed loss of volume of left hippocampus. V-EEG showed epileptic activity in the left temporal lobe without motor expression. Treatment consisted on IVIG, steroids and azathioprine, following cognitive improvement and dystonic seizures resolution. In both cases CSF was normal and antibody anti-LGI1 was positive in serum (titer=1/200) but negative in CSF (tested by cel-based-assay).

Conclusion: Anti-LGI1 encephalitis is a potentially severe condition, whose prognosis can improve with early diagnosis and immunosuppressive treatment. Although in typical cases dystonic seizures are faciobrachial, they can also involve the cervical region and lower limbs. Therefore, in the presence of dystonic seizures in any limb, this entity should be suspected, especially if the context of an abnormal EEG with no electrophysiological correlation with the symptoms.

Disclosure: No disclosure.

Motor neurone diseases 2

EPR-278

Electromyographic findings in primary lateral sclerosis: a follow-up study

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Background and aims: Primary lateral sclerosis (PLS) is a slowly progressive neurodegenerative disease affecting upper motor neurons (UMN) in adults. Electromyography (EMG) is essential to exclude significant lower motor neuron (LMN) involvement, but minor or transient changes may be present. Our aim was to characterize EMG findings in patients with PLS over time.
Methods: We retrospectively enrolled 20 patients with definitive diagnosis of PLS. Demographic features and functional progression (ALSFRS-R) were registered. We qualitatively scored the presence of spontaneous activity (fibrillation/sharp waves, fasciculation potentials) and motor unit potentials (MUAP) and compared it over time. We grouped patients according to lower (group 1) and higher (group 2) score of EMG abnormalities. A p-value <0.05 was considered significant.
Results: Fasciculation potentials were more common than fibrillation/sharp waves, (n=16 vs n=3), mainly in upper limbs. These abnormalities seemed to be stable or transitory. Abnormalities in MUAPs were found in most patients (n=16) with some worsening over time, particularly in lower limbs, but no statistically significant change was found. Compared to group 1 (n=7), patients in group 2 (n=13) were older at disease onset (median= 56 vs 40 years, p=0.023), and have shorter disease duration (median=10.4 vs 18.8 years, p=0.029).
Conclusion: In conclusion, most PLS patients show minor, stable or transitory EMG abnormalities. Patients with more evident EMG abnormalities are older and might have a faster disease progression. The impact of these findings on predicting progression to ALS is still to elucidate.
Disclosure: Nothing to disclose.

EPR-279

Longer-term improved/maintained motor function in nusinersen-treated children with later-onset SMA in CS2/CS12 and SHINE

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Background and aims: Nusinersen has demonstrated clinically meaningful efficacy in a broad population of individuals with SMA, including presymptomatic and symptomatic infants/children.
Methods: 28 participants with later-onset SMA (Type II or III) 1st received nusinersen in CS2 (NCT01703988), with 24 who completed treatment in CS12 (NCT02052791) and enrolled in the open-label SHINE study (NCT02594124). In SHINE, maintenance dosing was every six months until protocol amendment changed dosing to every four months. Outcomes included HFMSE and 6MWT.
Results: As of 27 August 2019, median (range) time on study was 6.3 (0.7–6.7) years for those with SMA Type II and 6.2 (0.08–6.8) years for those with SMA Type III. Mean (SD) HFMSE scores at baseline were 21.3 (9.5; n=11) and 48.9 (12.4; n=17) for participants with Type II and III, respectively. At Day 2010, HFMSE scores improved from baseline for participants with Type II (mean [SD] change at Day 2010: 9.6 [13.6; n=7]) and remained stable for those with Type III (-1.0 [7.5; n=9]). For Type III participants at Day 2010, 6MWT distance increased by a mean (SD) of 79.9 (41.7; n=7) meters from a baseline of 253.3 (182.7; n=13) meters. Among Type III participants, 83% (n/N=10/12) experienced clinically meaningful improvement (≥30 meters) in walking distance at Day 1770. One participant with SMA Type II gained the ability to walk independently following treatment with nusinersen. No new safety concerns were identified. Results from additional outcomes will be presented.
Conclusion: After a median of ~6 years' follow-up, participants with later-onset SMA demonstrated improvement or maintenance of motor function.
Disclosure: This study was sponsored by Biogen (Cambridge, MA, USA). Writing and editorial support for the preparation of this abstract was provided by Excel Scientific Solutions (Fairfield, CT): funding was provided by Biogen.

EPR-280

Nusinersen experience in adult patients with Spinal muscular atrophy in Greece.

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Background and aims: Nusinersen was the 1st approved treatment for intrathecal use in 5q spinal muscular atrophy (SMA) based on clinical trials in infants and children. Data regarding administration of nusinersen in adults are limited. We describe our experience in administrating nusinersen in adults patients.

Methods: 14 adult patients (type II=8, type III=6) (18-67 years old) with genetically confirmed SMA started treatment with Nusinersen, from 4/2019. A total of 78 lumbar punctures (LP) were carried out. All procedures were successful. In nine patients, the lumbar puncture was CT guided due to severe scoliosis or spondylodesis.

Results: There were no serious side effects besides post puncture syndrome. Totally 10/14 (71%) of patients reported either post LP headache (7.8%) or low back pain within 48 hours after LP (2,6%). Additionally, 2,6% of patients reported radiating pain. None of the patients has withdrawn treatment so far. Side effects such as coagulation abnormalities, thrombocytopenia, renal toxicity or hydrocephalus which have been recorded after administration of other subcutaneously or intravenously administered antisense oligonucleotides have not been observed.

Conclusion: Although the short follow up, nusinersen can be safely administrated in adult SMA patients, which makes the continuation of treatment necessary and imperative.

Disclosure: Nothing to disclose.

EPR-281

FIREFISH Parts 1 and 2: 24-Month Safety and Efficacy of Risdiplam in Type 1 SMA

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Background and aims: Spinal muscular atrophy (SMA) is a severe, progressive neuromuscular disease caused by reduced levels of survival of motor neuron (SMN) protein due to deletions/mutations of the SMN1 gene. A second gene, SMN2, produces only low levels of functional SMN protein. Risdiplam (EVRYSDI™), a centrally and peripherally distributed, oral SMN2 premRNA splicing modifier, received FDA approval for the treatment of patients with SMA, aged two months and older.

Methods: FIREFISH (NCT02913482) is a multicentre, open-label, 2-part study of risdiplam in infants with Type 1 SMA, and two SMN2 gene copies, aged 1–7 months at enrolment. Part 1 (n=21) assesses safety, tolerability and pharmacokinetics/pharmacodynamics of different risdiplam doses. Part 2 (n=41) assesses efficacy and safety of risdiplam at the dose selected in Part 1.

Results: Previously, we presented pooled data from 58 infants from FIREFISH Parts 1 (high-dose cohort, n=17) and 2 (n=41) who had received risdiplam for ≥12 months. At Month 12, 88% of infants were alive without permanent ventilation. Infants showed improvement in motor function, and achieved motor milestones such as sitting, standing and bouncing, not observed in natural history. There were no treatment-related adverse events leading to withdrawal. Here we present 24-month pooled FIREFISH data.
Conclusion: The safety and efficacy of risdiplam is consistent between FIREFISH Parts 1 and 2, incorporating a large population of infants from study sites that span a broad geographical area worldwide. FIREFISH Parts 1 and 2 are ongoing globally and will provide further efficacy and safety data on risdiplam in Type 1 SMA.
Disclosure: This study was sponsored by F. Hoffmann-La Roche Ltd, Basel, Switzerland. Writing and editorial assistance was provided by MediTech Media UK, in accordance with GPP3 guidelines, and funded by F. Hoffmann-La Roche Ltd.

EPR-282

RAINBOWFISH: A study of risdiplam in infants with presymptomatic SMA

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Background and aims: Spinal muscular atrophy (SMA) is a severe, progressive neuromuscular disease caused by reduced levels of survival of motor neuron (SMN) protein due to deletion/mutations of the SMN1 gene. A second gene, SMN2, produces only low levels of functional SMN protein. Risdiplam (EVRYSDI™), a centrally and peripherally distributed, oral SMN2 premRNA splicing modifier received FDA approval for the treatment of patients with SMA, aged two months and older.
Methods: RAINBOWFISH (NCT03779334) is an open-label, single-arm, multicentre global clinical study enrolling infants aged from birth–6 weeks of age (at 1st dose), regardless of SMN2 copy number. Infants will receive risdiplam for 24 months, followed by a 36-month extension. Primary analysis will be conducted after 12 months of treatment in infants with two SMN2 copies and compound muscle action potential (CMAP) amplitude ≥1.5mV at baseline.
Results: The primary endpoint is the proportion of infants sitting without support for ≥5 seconds after 12 months of treatment (assessed by the Bayley Scales of Infant and Toddler Development, Third Edition). Secondary endpoints include the development of clinically manifested SMA, measures of survival, motor function and growth, nutritional status, CMAP, pharmacokinetics, and safety monitoring. The median age at 1st dose (range) for the first seven enrolled infants was 35 (16–40) days. We will report updated baseline demographics and baseline SMN protein data in enrolled infants with presymptomatic SMA. Additional preliminary data will also be presented.
Conclusion: RAINBOWFISH will provide valuable information about presymptomatic administration of risdiplam. Recruitment for the study is ongoing worldwide.
Disclosure: This study was sponsored by F. Hoffmann-La Roche Ltd, Basel, Switzerland. Writing and editorial assistance was provided by MediTech Media UK, in accordance with GPP3 guidelines, and funded by F. Hoffmann-La Roche Ltd.

EPR-283

JEWELFISH: 12-month safety, pharmacodynamic and exploratory efficacy of risdiplam in non-naïve patients with SMA

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Background and aims: Spinal muscular atrophy (SMA) is a severe, progressive neuromuscular disease caused by reduced levels of survival of motor neuron (SMN) protein due to deletions/mutations of the SMN1 gene. A 2nd gene, SMN2, produces only low levels of functional SMN protein. Risdiplam (EVRYSDI™), a centrally and peripherally distributed, oral SMN2 pre-mRNA splicing modifier, received FDA approval for the treatment of patients with SMA, aged two months and older.
Methods: JEWELFISH (NCT03032172) is a multicentre, open-label study evaluating the safety, tolerability and pharmacokinetics and pharmacodynamics (PD) relationship of daily oral risdiplam in non-naïve (previously treated with other SMA therapies) patients with SMA. JEWELFISH participants have previously received nusinersen (SPINRAZA®), onasemnogene abeparvovec-xioi (ZOLGENSMA®), olesoxime or RG7800 (RO6885247).
Results: The JEWELFISH patient population included a broad range of ages (1–60 years), SMA types (1–3), and SMN2 copy numbers (1–5). Safety data from 173 patients (data-cut: 31st January 2020) who received risdiplam for up to 32.8 months showed no treatment-related safety findings leading to withdrawal. The overall safety profile of risdiplam treatment in non-naïve patients was consistent with that of treatment-naïve patients (SUNFISH [Types 2/3, NCT02908685]; FIREFISH [Type 1, NCT02913482]). PD data showed a ≥2-fold increase in median SMN protein levels versus baseline (data-cut: 1st June 2020), consistent with treatment-naïve patients. We will present 12-month safety, PD and exploratory efficacy data from JEWELFISH.
Conclusion: JEWELFISH is ongoing across Europe and the US and will provide important data on the safety, PD and exploratory efficacy of risdiplam in a heterogenous population of non-naïve patients with SMA.
Disclosure: This study was sponsored by F. Hoffmann-La Roche Ltd, Basel, Switzerland. Writing and editorial assistance was provided by MediTech Media UK, in accordance with GPP3 guidelines, and funded by F. Hoffmann-La Roche Ltd.

EPR-284

Pooled safety data from the risdiplam clinical trial development program

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Background and aims: Spinal muscular atrophy (SMA) is a severe, progressive neuromuscular disease caused by reduced levels of survival of motor neuron (SMN) protein due to deletions/mutations of the SMN1 gene. A 2nd gene, SMN2, produces only low levels of functional SMN protein. Risdiplam (EVRYSDI™), a centrally and peripherally distributed, oral SMN2 pre-mRNA splicing modifier, received FDA approval for the treatment of patients with SMA, aged two months and older.
Methods: The risdiplam programme consists of four studies across a broad SMA population: • FIREFISH (NCT02913482): a 2-part study assessing safety, tolerability, pharmacokinetics (PK), pharmacodynamics (PD) and efficacy in infants with Type 1 SMA (inclusion criteria: 1–7

months at enrolment) • SUNFISH (NCT02908685): a 2-part study assessing safety, tolerability, PK, PD and efficacy in patients with Type 2 or 3 SMA (inclusion criteria: 2–25 years at enrolment) • JEWELFISH (NCT03032172), assessing safety, tolerability, PK and PD in patients with SMA (inclusion criteria: six months–60 years at enrolment) who previously received RG7800 (RO6885247), nusinersen (SPINRAZA®), olesoxime or onasemnogene abeparvovec-xioi (ZOLGENSMA®) • RAINBOWFISH (NCT03779334), assessing efficacy, safety, PK and PD in infants (inclusion criteria: birth–6 weeks at first dose) with genetically diagnosed and presymptomatic SMA.

Results: Pooled analyses from FIREFISH Parts 1 and 2, SUNFISH Parts 1 and 2 and JEWELFISH showed no treatmentrelated safety findings leading to withdrawal from risdiplam treatment of up to 39 months in 465 patients (data-cut: 15th January 2020). Here, we present updated pooled safety analyses for risdiplam.

Conclusion: This analysis will add to the understanding of the long-term safety profile of risdiplam.

Disclosure: This study was sponsored by F. Hoffmann-La Roche Ltd, Basel, Switzerland. Writing and editorial assistance was provided by MediTech Media UK, in accordance with GPP3 guidelines, and funded by F. Hoffmann-La Roche Ltd.

EPR-285

Understanding Clinical Heterogeneity in Amyotrophic Lateral Sclerosis (ALS) – A Systematic Literature Review

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Background and aims: Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease. While ALS is uniformly life-shortening, its time-course and clinical features can be variable. The objective of this study was to describe the heterogeneity in ALS diagnosis, patient characteristics, functional decline, and survival.

Methods: A systematic literature review (SLR) was conducted using predefined search criteria. Observational and registry studies published in English from 06/2010–08/2020 were reviewed for outcomes including age of onset and diagnosis, diagnostic delay, functional status and decline, and survival. The median of reported median values and ranges are used to present the data in aggregate.

Results: This SLR assessed 2,493 citations, ultimately including 258 citations (Figure 1). In studies that reported on general ALS populations (173 citations), spinal/limb onset was the most prevalent (between 37–86%), followed by bulbar onset (between 6–56%) (Figure 2). The median age of ALS symptom onset was 62 years (range 14–90 years). The median age of ALS diagnosis was 67 years (range 17-–90 years). Median diagnostic delay, the time between symptom onset and diagnosis, was 11 months with studies reporting median delays of 7–22 months. Between 15–20 months from symptom onset, ALSFRS-R scores ranged from 31–40, with increasing variability over time (Figure 3). Median survival from symptom onset was 3.3 years, with studies reporting median survival of 1.5-5.3 years.

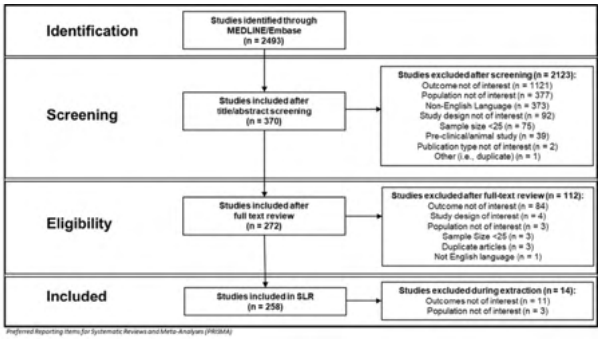

Figure 1: PRISMA Diagram

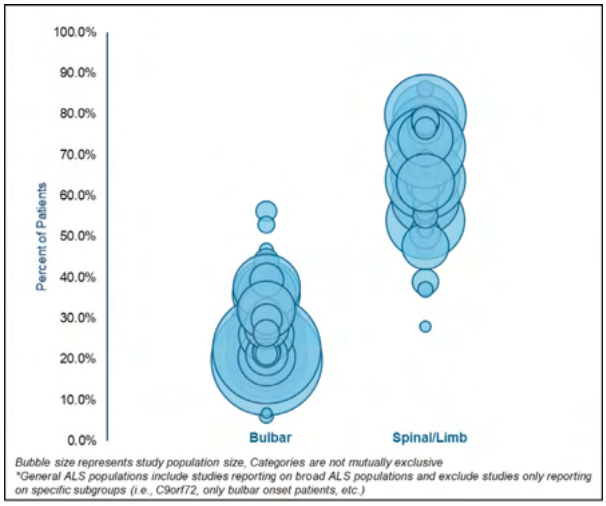

Figure 2: Site of Onset in General ALS Populations*

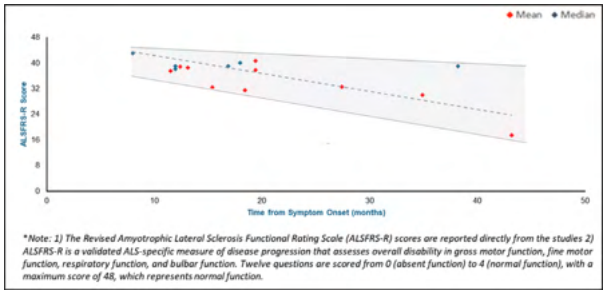

Figure 3: Disease Progression (ALSFRS-R) from Symptom Onset*

Conclusion: The heterogeneity in ALS presentation may contribute to the complexity and delays in diagnosis. Strategies supporting earlier diagnosis are needed to ensure early intervention and improved outcomes for patients living with this progressive, life-shortening disease.
Disclosure: This research was funded by Biogen, Inc.

EPR-286

An Italian patient with Amyotrophic Lateral Sclerosis and Myasthenia Gravis: a clue for the dying-back hypothesis

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Background and aims: Symptoms of Amyotrophic Lateral Sclerosis (ALS) and Myasthenia Gravis (MG) may overlap, causing misdiagnosis at disease onset. More rarely, the two diseases can coexist. Here we report the case of a 59-years-old patient who was diagnosed for MG in 2013 due to the occurrence of diplopia, dysphagia, positive acetylcholine receptor antibodies, and typical electromyogram. The patient came to our attention in June 2020 for progressive left lower limb hyposthenia, cramps and fasciculation. Interestingly, he also had suffered from sarcoidosis in the past.
Methods: The patient underwent a complete neurological examination, serum and instrumental analyses at Santa Chiara Hospital, Pisa.
Results: Electromyogram showed a neurogenic pattern in deltoid, finger extensor, and tibialis anterior muscles, with fasciculation potentials in upper limbs muscles and in vastus medialis muscles bilaterally. High camp brain MRI showed bilateral corticospinal tract hyperintensity. Anti-nerve and anti-neuron antibodies resulted negative, excepting for SOX1 antibodies resulted positive. Complete paraneoplastic screening resulted negative. The neurological examination showed upper and lower limbs hyposthenia with slight proximal hypotrophy, diffuse fasciculations, brisk deep tendon reflex, positivity of Hoffmann signs bilaterally and left Babinski sign.
Conclusion: The results suggest that the patient, known for suffering from MG, developed also ALS. The presence of SOX1 antibodies, known to cause neuromuscular junction diseases, may support the role of dysimmunity in pathogenesis of motor neuron diseases, underlying the fact that muscles and neuromuscular junctions may be sites of disease manifestation in early stage of ALS, supporting what is called the “dying-back” hypothesis.
Disclosure: The Authors declare no conflict of interest

Neuroepidemiology

EPR-287

Epidemiology of acute flaccid paralysis and vaccination coverage in Rio Grande do sul state, Brazil

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Background and aims: Acute Flaccid Paralysis or polio is a viral infectious disease that affects the motor neurons of the central nervous system and can be prevented through vaccination. This study aimed to describe the number of acute flaccid paralysis cases and to identify the relationship with vaccination coverage in the State of Rio Grande do Sul, Brazil.
Methods: An ecological study was carried out in January 2021 from the health information of the Brazilian Health Unified System databases. The analysis comprised the number of notified cases and the % of vaccination coverage from 2010 to 2019 in seven health macro-regions (Vales, Sul, Serra, Norte, Missioneira, Metropolitana, and Centro Oeste) in the state of Rio Grande do Sul, Brazil. Descriptive statistics were performed through absolute (n) and relative (%) frequencies.
Results: A total of 234 cases of polio were reported, with an increase from three cases in 2010 to 34 in 2019. At the same period, had a decrease in the percentage of polio vaccination coverage in the State, from 92.3% in 2010 to 83.5% in 2019. The Missioneira region has the lowest numbers of cases in the period (n=8), with a percentual vaccination coverage close to 100%. The highest number of absolute cases was at the Metropolitana region (n=123), with vaccination coverage of 86%.
Conclusion: We observed a relationship between the increase in polio cases and the decrease in vaccination coverage. Thus, it is necessary to seek the minimum vaccination coverage goal recommended by the World Health Organization – ≥95%.
Disclosure: No disclosure.

EPR-288

Leprosy in Brazil: Notifications from 2010 to 2019

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Background and aims: Leprosy is a chronic disease, caused by the bacterium Mycobacterium leprae. It is characterized by a decrease or loss of thermal, pain, tactile sensitivity, and muscle strength. This study aimed to describe the characteristics of Brazilians with leprosy.
Methods: An ecological study was carried out in January 2021 from the health information of the Brazilian Health Unified System databases. The analysis comprised the number of notified cases in Brazil from 2010 to 2019. The main variables analyzed were: sex, skin color, age, education, a region of notification, and diagnostic operational class. Descriptive statistics were performed through absolute (n) and relative (%) frequencies.
Results: A total of 379,050 leprosy cases were reported, with a decrease from 42,636 in 2010 to 36,965 in 2019. Most patients were male (57%), with brown skin color (56%), aged between 50 and 59 years (18%), and incomplete elementary education (22%). In the distribution by region of the country, it was observed that 42% of the total occurred in the Northeast, 19% in the North, 19% in the Midwest, 15% in the Southeast, and 3% in the South. The most prevalent diagnostic operational class was the multibacillary (71%).
Conclusion: There was a total decrease in leprosy cases in Brazil, but there is still vulnerability to this disease in some regions, such as in the Northeast of Brazil. Therefore, prevention and early detection of the disease must be encouraged to combat this public health problem.
Disclosure: No disclosure.

EPR-289

Medically unexplained symptoms and functional neurological disorders in a Neurology ward, a retrospective study

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Background and aims: Medically unexplained symptoms (MUS) account for up to one third of the consultations in Neurology. Current research shows that functional neurological disorders (FND) may be involved in a significant proportion of these. Adequate communication of diagnosis and therapeutic management has prognostic implications.

Methods: Retrospective analysis of admissions to Neurology from September 2019 to May 2020, with diagnosis of MUS. Discharge reports were analyzed, applying ICD-11 diagnostic criteria of FND and collecting demographic and clinical variables.

Results: In nine months, 27 patients with MUS (9% total admissions) were included. They were divided according to discharge diagnosis into three groups: (1) positive diagnosis of FND (29.63%), (2) MUS with ICD-11 criteria but no positive diagnosis of FND (33.33%) and (3) MUS with absence of data suggesting FND (37.04%). Comparing group 1 with 2, the positive diagnosis of FND was associated to higher percentages of incongruity (100%; 77.7%), inconsistency (62.5%; 55.56%), positive signs in the examination (μ=3,125±1.06; μ=0.89±0.92) and number of complaints (μ=4,125±1.13; μ=3±1.58); and with less coexistence of other neurological diseases (12.5%; 55.5%) and less number of new symptoms (50%; 77.5%). Group 3 did not present any criteria of FND and also associated a lower number of complaints (μ=1.5±0.71). There were no differences in psychiatric comorbidity between the three groups.

Conclusion: A significant proportion of MUS meet FND criteria, only a subset of them receiving a diagnosis. The reasons for the absence of diagnosis are new symptoms and coexistence with other pathologies. Their correct identification and treatment could modify the prognosis in selected patients.

Disclosure: Nothing to disclose.

EPR-290

Prognostic factors related to the risk of COVID-19 infection in MS patients

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Background and aims: It is still debated whether Multiple Sclerosis (MS) patients are at high-risk of COVID-19 because of their life style, disease- or treatments-associated immune alterations. We compared features of MS patients with COVID-19 infection (MS-COVID) to those of residency-, age-, sex- and treatment-matched MS controls (MS-NCOVID). Moreover, the severity of COVID-19 infection was assessed in MS-COVID patients and their cohabitants.

Methods: So far, we have enrolled 25 MS-COVID and 104 MS-NCOVID patients. Neurological examination, premorbid laboratory tests, anthropometric variables (height, weight and BMI), life-style habits (smoke, alcohol intake, diet), working-activity and living conditions (number of cohabitants, school-aged children) were assessed. COVID-19 severity was evaluated in terms of fever (magnitude, duration), radiological pneumonia and typical symptoms.

Results: Clinical and anthropometric features, life-style habits and living conditions were similar between MS-COVID and MS-NCOVID patients. However, they differed in terms of working activity, with lower rate of unemployment (7.1% vs 23.4%) and higher rate of team-working (61.5% vs 26.5%) in the MS-COVID group ($p<0.01$). Furthermore, MS-COVID patients had lower premorbid vitamin D levels (31 vs 40ng/ml p=0.048) and higher neutrophils count (3,803 vs 3,182 cells/ul, p=0.046). Disease course was similar between MS-COVID patients and their cohabitants with fever, ageusia and anosmia being the most common symptoms. Fever and radiologic signs of pneumonia were also comparable.

Conclusion: Working-activity, lower vitamin D levels and higher neutrophil count seem to be associated with the risk of COVID-19 infection in MS patients. The burden of COVID-19 disease was comparable between MS patients and their cohabitants.

Disclosure: Authors report no conflict of interest relevant for this study.

EPR-291

Multiple sclerosis and migration: ethnic, cross-cultural and phenotype differences from a multicenter study in Italy

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Background and aims: The aim of this study was to compare the phenotype characteristics of MS patients living in Italy and born in different countries.

Methods: We collected data from 1,360 individuals affected by MS (458 foreign-born and 902 age- and sex-matched native-born Italian patients). We compared clinical data at disease onset, diagnosis, and follow-up through different comparisons: Country of origin; income of the Country (high-income countries vs. low-middle); geographical areas of origin. Analyses considered continuous variables as mean, median and interquartile range. Multivariate logistic models were also built calculating OR and 95% CI..

Results: Sex ratio and relapse frequency were not significantly different in all kind of comparisons. MS individuals born in higher income Countries had a lower disability at onset compared to those from low-medium income Countries (OR 0.31; CI 0.16–0.64; $p \leq 0.001$). Pyramidal involvement at presentation (OR 0.48; CI 0.30–0.78; p=0.002), and sphincteric symptoms (OR 0.11; CI 0.03–0.46; p=0.0001) were less frequent among patients coming from higher income Countries compared to the others. MRI lesion load at diagnosis (OR 0.31; CI 0.12–0.67; p=0.002) and progression since disease onset (OR 0.52; CI 0.36–0.73; $p<0.001$) were inversely associated both to higher income Country origin as well as to a Caucasian ancestry.

Conclusion: The present study indicates that not only ethnic group belonging, but also socio-demographical differences in HealthCare facilities for people with MS born in different countries are associated to diversities in phenotype characteristics and need therefore to be considered in the management of individuals with MS.

Disclosure: Dr. Paolo Ragonese has received grants from Roche and Almirall, and honoraria from Biogen, Merck, Novartis, and Roche.

EPR-292

Antiherpetic medication and incident dementia: observational cohort studies in four countries

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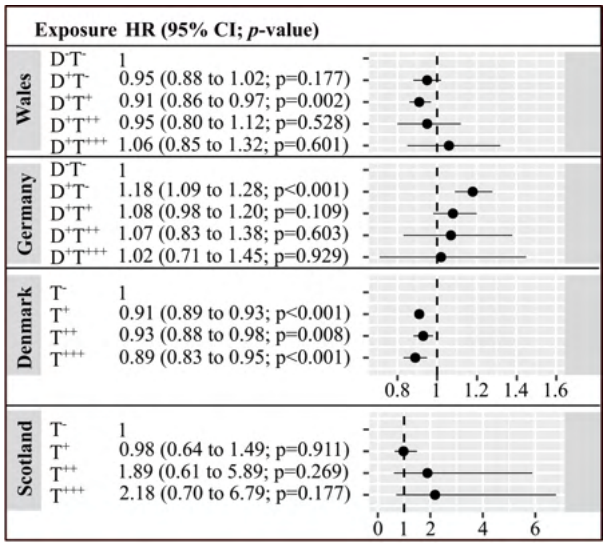
Background and aims: Several epidemiological studies from Taiwan, all using the same data source, found significant associations between herpes virus infection, antiherpetic medication, and dementia. We conducted an observational cohort study using health registry data from Wales, Germany, Scotland, and Denmark to investigate potential associations between antiherpetic medication and incident dementia, broken down according to medication type and dose, type of herpes virus, and dementia subtype.

Methods: 2.5 million people aged 65 and older were followed up using routinely collected linked electronic health records in four separate national observational cohort studies. Exposure and outcome were classified using coded data from prescriptions and from primary and secondary care. Data were analyzed using survival analysis with time-dependent covariates. Confounders were age, year, sex, socioeconomic status, and comorbidities.

Results: Results were heterogenous across cohorts, with a tendency for decreased dementia risk in people exposed to antiherpetic medication (Figure 1). Associations were not affected by number of treatments, herpes diagnosis, type of dementia, or specific type of medication. People diagnosed with herpes but not exposed to antiherpetic medication were at higher dementia risk in the German cohort but not in the Welsh cohort (Figure 1).



Adjusted Hazard Ratios and confidence intervals for the association of herpes diagnosis and exposure to antiherpetic medication with dementia. D- not diagnosed; D+ diagnosed; T- not medicated; T+ medicated once; T++ medicated twice; T+++ medicated 3.

Conclusion: Results from the four large cohorts allow us to exclude any major assocation of short-term exposure to antiherpetic medication with dementia. Because neither type of dementia nor type of herpes infection modified the association, the small but significant decrease in dementia incidence with antiherpetic adminstration may reflect unmeasured confounding and misclassification.

Disclosure: All co-authors declare no conflict of interest.

Clinical neurophysiology

EPR-293

Continuous EEG to detect recognition of next-of-kin by unresponsive patients, suggesting preserved consciousness

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Background and aims: Consciousness levels in clinically unresponsive patients are misdiagnosed in 15–20%, which might lead to inaccurate prognostication. Electroencephalography (EEG) is widely used in unresponsive patients to assess brain activity and reactivity. Auditory stimulation by calling patients by their name can elicit a robust EEG response. Continuous EEG (cEEG) combined with stimulation by next-of-kin (an emotionally salient stimuli) has not been evaluated for detection of preserved consciousness in patients with acute brain injury. In this ongoing study, our objective is to investigate if preserved consciousness can be detected more often in clinically unresponsive patients with acute brain injury, using cEEG, when stimuli are applied by next-of-kin compared to health professionals.

Methods: Adult unresponsive patients with acute brain injury from ICU are being assessed by cEEG while being alternatingly addressed by a next-of-kin and a health professional. EEG reactivity in response to stimuli is assessed visually and with automated measures for comparison (Fig. 1).

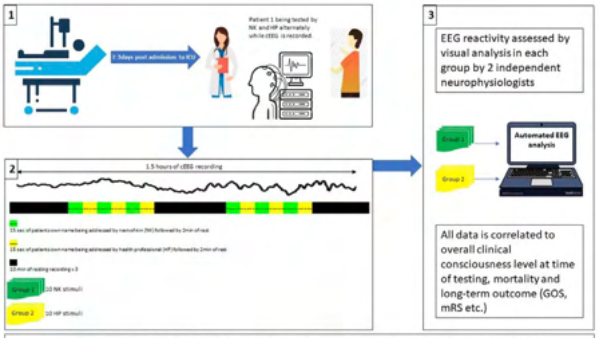

Figure 1: Flow of patients through the study from time of inclusion (1), cEEG recording (2) and analysis of obtained data (3).
Abbreviations: ICU: Intensive Care Unit, cEEG; Continuous electroencephalography, NK: next-of-kin, HP; Health professional, GOS; Glasgow outcome scale, mRS; Modified rankin scale.

Figure 1

Results: As of 12/2020, 15 patients were included. All were addressed 10 times by next-of-kin and a health care professional (table 1). Preliminary results show that in seven patients (46.7%), EEG reactivity was more frequent in response to next-of-kin, while in five patients (33.3%) reactivity was more evident in response to the health professional. No difference was observed in three patients.

Table 1. Basic characteristics of patients

Characteristics	All Patients (*N=15*)
Male – no. (%)	9 (60)
Age, years	
- Mean (SD)	62.8 (8.9)
Cause of admission to ICU – no. (%)	
- TBI	3 (20)
- SAH	3 (20)
- ICH	3 (20)
- CA	4 (27)
- Other	2 (13)
Duration of cEEG recording – Minutes	
- Mean (SD)	85.7 (10.1)
Sedation during EEG recording – no. (%)	
- None	8 (53)
- Low level Remifentanil	7 (47)
Clinical consciousness level at time of recording – no. (%)	
- UWS	4 (27)
- MCS-	8 (53)
- MCS+	3 (20)

Abbreviations:
SD; Standard deviation, ICU; Intensive Care Unit, TBI; Traumatic brain injury, SAH; Subarachnoid hemorrhage, ICH; Intracerebral hemorrhage, CA; Cardiac arrest, cEEG; Continuous electroencephalography, UWS; Unresponsive wakefulness state, MCS-; Minimal conscious state minus, MCS+; Minimal conscious state plus

Table 1

Conclusion: Our preliminary results may indicate that a subset of clinically unresponsive ICU patients with acute brain injury show increased EEG reactivity more often when approached by a next-of-kin, possibly implying recognition of a familiar voice and thus preserved consciousness.

Disclosure: Nothing to disclose.

EPR-294

Neuromodulatory effects of motor cortex theta burst stimulation

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Background and aims: The combined use of electroencephalography (EEG) and transcranial magnetic stimulation (TMS) is used to assess effects of theta burst stimulation (TBS) on cortical excitability. Based on prior literature TBS predominantly affects N100 amplitude, with opposite effects induced by continuous TBS (cTBS) versus intermittent TBS (iTBS). N45 and N100 components have been linked to intracortical inhibitory processes related to GABAa or GABAb.
Methods: We conducted a neuronavigated, sham-controlled study in fifteen healthy subjects investigating modulation of motor cortex TMS-evoked potentials (TEPs) before and after cTBS, iTBS or sham stimulation over the motor cortex.
Results: N100 amplitude showed a significant condition effect, with reduction by active stimulation compared to sham. LMFP (local mean field potential) analysis showed significant reduction around 100ms by the active stimulation conditions. Significant LMFP reductions were also found at 6–7ms and 71–79ms for cTBS and at 56–63ms for iTBS. A trend toward N45 increase occurred following cTBS and iTBS versus sham. LMFP around 180ms was found significantly increased in the sham condition, whereas this was absent following active stimulation. DI (divergence index) analysis identified significant differential effects of iTBS versus sham and a trend toward significance for cTBS versus sham in the 0–70ms window.
Conclusion: TBS over the motor cortex was found to reduce N100 and potentially increase N45 amplitude, irrespective of the applied TBS paradigm. Analysis within the early time window (0–70ms) did reveal some differential effects on LMFP. We postulate that the effect of TBS on cortical excitability is related to GABAa-ergic effects considering evidence from pharmaco-TMS-EEG studies.
Disclosure: Nothing to disclose.

EPR-295

Scale Invariance in the Sleep-Wakefulness Rhythm: Detrended Fluctuation Analysis Applied to the EEG Odds-Ratio Product

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Background and aims: Sleep stages are not periodic; rather, high variability can be found among different subjects or even for the same sleeper over different nights. The intricacies of neuronal sleep activity continue to be actively investigated. This study explored aspects of scale invariance applied to sleep stage succession.
Methods: Odds-ratio-product (ORP) values were obtained from high density EEG tracings (73 channels) pertaining to subjects previously diagnosed with either epilepsy or psychogenic nonepileptic events (PNEE). ORP is a measure of sleep depth, relying on the relative power each frequency band contributes to surface electroencephalography (EEG) signal. ORP values range between 0 – a state of deep sleep – and 2.5 – a state of full wakefulness. ORP time series were analyzed using detrended fluctuation analysis (DFA) in order to quantitatively characterize their time scale invariance properties. The resulting scaling exponent H, ranging between 0 and 1, indicates the degree of time series persistence.
Results: Time scale invariance was identified for all subjects and all electrodes studied, both in wakefulness and sleep. Moreover, the time scale invariance measure characterized by the H exponent revealed consistent patterns associated with electrode regions. The study also revealed stronger similarities regarding scale invariance patterns in PNEE subjects compared to epilepsy subjects.
Conclusion: The study revealed time scale invariance properties in sleep stage succession reflected in ORP values. To our knowledge, this has not been previously described. Such an approach may thus shed light on underlying sleep / wakefulness rhythm physiology and further develop our understanding of sleep related pathology.
Disclosure: Nothing to disclose.

EPR-296

Nerve Ultrasound in CIDP: Correlation with Clinical Features, Electrophysiology and Functional Disability

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Background and aims: Increased nerve cross-sectional area (CSA) is a characteristic ultrasonographic finding in CIDP. We aim to evaluate the ultrasound features of peripheral nerves in CIDP and their correlation with clinical characteristics, electrophysiology and functional disability.
Methods: CIDP patients fulfilling the EFNS/PNS criteria were recruited. All patients underwent neurological assessment with MRC sum score, grip strength, INCAT disability score, and also had nerve conduction studies and ultrasound, using a standardized protocol.
Results: 22 patients (15M:7F) with mean age 51.5±17.9 years were included. Disease duration ranged from two months to 10 years (mean 2.2±2.4 years) and CSF protein ranged from 0.65 to 11.32 g/L (mean 2.22±2.45). Mean MRC sum score was 51.5±7.7, grip strength 14.1±8.6 kg and INCAT 5.2±2.3. Increased nerve CSAs was detected in 70% of the 369 nerve segments. The ulnar forearm ($r=0.640$, $p=0.001$) and sural nerve ($r=0.661$, $p=0.001$) CSAs significantly correlated with disease duration. CSF protein correlated with median elbow and midarm CSAs ($r=0.834$–0.859, $p<0.001$); all ulnar ($r=0.702$–0.898, $p\leq0.001$–0.001), fibular ($r=0.835$–0.958, $p<0.001$), tibial ($r=0.770$–0.820, $p\leq0.001$–0.001) and radial ($r=0.548$, $p=0.019$) CSAs. INCAT score correlated significantly with fibular CSAs ($r=0.506$–0.673, $p=0.002$–0.027). Correlation analysis with electrophysiology found increased nerve CSAs correlated with DML (median wrist to midarm: $r=0.535$–0.732, $p\leq0.001$–0.013; ulnar wrist, forearm and midarm: $r=0.627$–0.878, $p=<0.001$–0.002) and MCV (median elbow and midarm: $r=-0.485$–0.517, $p=0.023$–0.035; ulnar forearm: $r=-0.462$, $p=0.046$).
Conclusion: In CIDP, nerve CSAs are increased at most sites and can demonstrate significant correlation with disease duration, CSF protein, disability and electrophysiology. Nerve ultrasound can be useful as a further disease biomarker in CIDP.
Disclosure: The authors have Nothing to disclose..

EPR-297

Circadian and ultradian rhythms depend on the level of consciousness in disorders of consciousness

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Background and aims: Eye opening in patients with disorders of consciousness (DOC) marks the onset of a cyclic pattern with and without arousal. In minimally conscious state (MCS) arousal may be accompanied with awareness, unlike in unresponsive wakefulness syndrome (UWS). The presence of circadian and/or ultradian rhythmicity in patients with DOC has not been well established. To this end, we analyzed actigraphy data with a method well-suited to account for the variable rhythms within and across days observed in this population.
Methods: We collected actigraphy data from 73 subjects (19 controls, 35 MCS, 19 UWS) over seven days and performed analyses using PyActigraphy. Singular Spectrum Analysis, a data-driven technique, was used to decompose the signal into circadian and ultradian rhythms. Next, we will evaluate these results statistically and correlate patients' clinical diagnoses using the Coma Recovery Scale-Revised with the phase of detected circadian rhythms.
Results: Data cleaning resulted in exclusion of one control (5.3%), 10 MCS (28.6%) and nine UWS (45%) subject(s). Our preliminary results show that the strength of circadian and ultradian rhythms in actigraphy data decreases with consciousness from healthy controls to MCS and almost disappearing in UWS (Figure 1).

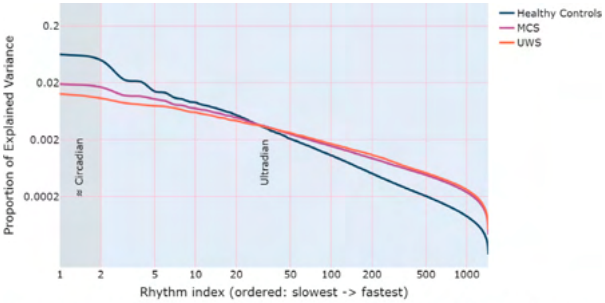

Figure 1: Actigraphy variance explained by increasingly fast rhythms in the data. Linear lines would show no rhythms standing out, while staircase-like lines denote the presence of dominant rhythms. The slowest rhythms (indexes 1-2) will be the ones closest to a 24h cycle (i.e., the circadian rhythm), but Singular Spectrum Analysis does not restrict the period of the signal. Follow-up analyses will provide the mean rhythms associated with these indexes. Other indexes show increasingly fast ultradian rhythms. Healthy controls (n=18) show the clearest staircase-like line, resulting from a clearly present circadian rhythm and some ultradian components. This pattern is still slightly present in minimally conscious state (MCS) patients (n=25), at least for a circadian component, but appears to be largely absent in unresponsive wakefullness syndrome (UWS) patients (n=10). Future analyses will statistically evaluate these differences.

Conclusion: Preservation of circadian/ultradian rhythms seems associated with the level of consciousness. Rhythms appear almost absent in UWS patients, which suggests limited behavioral evidence for a sleep/wake cycle although eye opening is observed. Overall, the use of actigraphy could contribute to clinical assessments in DOC, and although data quality might be suboptimal, acquisition can be repeated easily.
Disclosure: The authors have Nothing to disclose..

Cognitive neurology/neuropsychology 2

EPR-298

A smartphone-app for risk factor management improves physical activity in young ischemic stroke patients

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Background and aims: Efficient treatment of modifiable risk factors such as arterial hypertension, smoking, obesity and dyslipidemia decreases reoccurrence of ischemic stroke. In this pilot study, we assessed the effect of a newly developed smartphone-app for secondary stroke prevention supporting risk factor management. We focused on young ischemic stroke patients, as this cohort would most strongly benefit from beneficial effects.
Methods: The app conveys key facts about stroke in a comprehensible lay format, provides motivational support for a healthy lifestyle (physical activity, healthy nutrition, smoking cessation) and a reminder function for medication intake and blood pressure measurement. Between January 2019 and February 2020, we consecutively invited ischemic stroke patients aged between 18 to 55 years to participate.
Results: The current sample comprises 21 patients in the app-intervention group (62% male; age=41±11 years; education=12±3 years) and 21 sex-, age- and education-matched ischemic stroke patients in the control-group (57% male; age=47±8 years; education=11±3 years). Baseline stroke severity was comparable between groups (p=0.883) and improved within three months post-stroke (median NIHSS at baseline=4 (1–6) and follow-up=0 (0–1); p<0.001). Two-thirds of the intervention-group used the support for physical activity and healthy nutrition and one-quarter quitted smoking. 90% reported "high" or "very high" overall satisfaction. Three months post-stroke, app-users were physically almost twice as active (13±9 hours/week) compared to controls (7±5 hours/week; p=0.022). Nutritional (p=0.009) and smoking behaviour (p=0.001) improved in both groups three months post-stroke.
Conclusion: Young ischemic stroke patients were highly satisfied with our newly developed smartphone-app and profited from motivational support leading to increased physical activity.
Disclosure: Nothing to disclose.

EPR-299

Application of the at(n) system in posterior cortical atrophy: a case series

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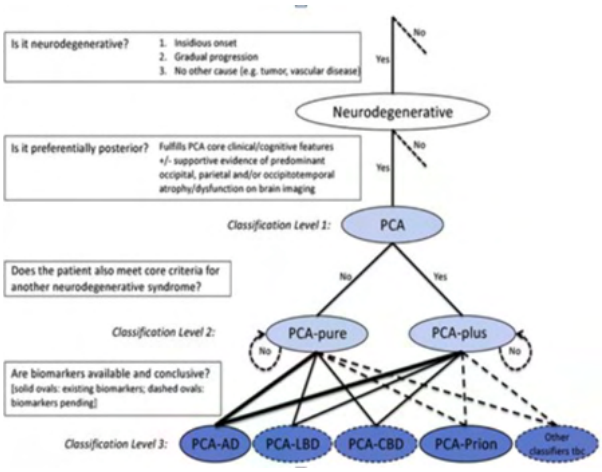
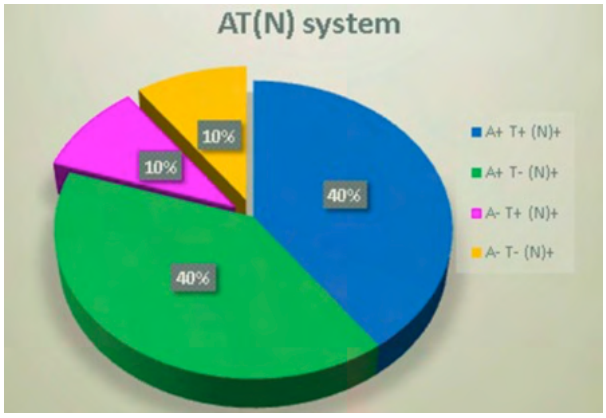
Background and aims: Posterior cortical atrophy (PCA) is a rare syndrome with prominent visuospatial deficits characterized by atrophy of the parietal and/or occipital lobes. In most patients, PCA is attributable to Alzheimer's disease (AD) according to pathological studies. However, Lewy body dementia, Corticobasal degeneration and prion disease (Heidenhain variant) are rarer alternative underlying pathologies. In this study, CSF biomarker profiles were studied in a case series of 10 PCA cases and the AT(N) classification system was applied.

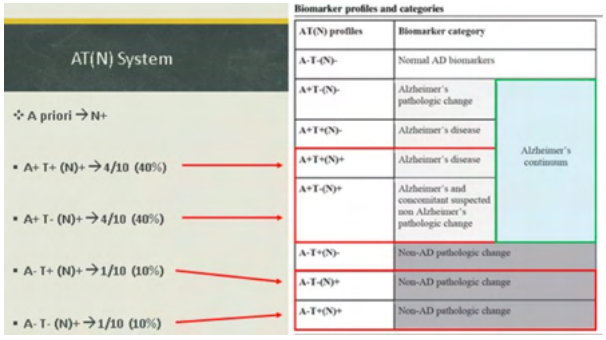


PCA classification

Methods: Data were collected retrospectively, from the Parkinson-plus Registry of our Department. A total of 10 patients, hospitalized between 2000 and 2019 fulfilling diagnostic criteria for PCA, were included. All patients underwent extensive clinical, neuropsychological and imaging (brain MRI and HMPAO-Spect) investigations. Classical CSF AD biomarkers (total tau, phosphorylated tau and -amyloid) were measured and each patient was classified based on the AT(N) system.
Results: Mean age of onset was 58 years and 60% of patients were female. 80% of patients had an "Alzheimer's continuum" neurochemical profile, with 40% classified as "Alzheimer's disease" (A+T+N+). The biochemical profile of the remaining 20% of cases was compatible with "non-AD pathologic change" (A-T+N+).



Classification of patients according to ATN scheme



Biomarker profiles and categories

Conclusion: Application of the AT(N) system classifies the majority of PCA cases examined in the "Alzheimer's continuum" category. These findings are in accordance with pathological studies, highlighting the importance of CSF biomarkers in the in vivo diagnosis of this rare syndrome.
Disclosure: The authors declare that they have no conflict of interest.

EPR-300

Utility of the FTLD-modified CDR in the Portuguese population: preliminary results

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Background and aims: The Clinical Dementia Rating Scale (CDR), initially designed to quantify the severity of dementia, is also useful to assess disease progression in Alzheimer's disease (AD). The FTLD-modified CDR (FTLD-CDR) was developed by adding to the CDR two extra domains focused on the main features of FTD: Language and Behavior/Comportment/Personality. Since there are no validated instruments to estimate disease staging and progression in FTD in our country, we adapted and validated the FTLD-CDR in our clinical-setting and language.
Methods: Cross-sectional study conducted with 25 behavioral variant-FTD (bvFTD) and 25 AD patients matched for (Mini Mental State Examination) MMSE, age and disease duration. Patients were diagnosed according to the most recent international criteria and underwent a thorough neurological, neuropsychological, biochemical (CSF-biomarker) and imaging (amyloid-PET) evaluation. A translated and adapted version of the scale was administered by a blinded neuropsychologist who interviewed patients together with their caregivers.
Results: There were no differences between groups regarding age-at-onset and education. AD patients had lower baseline FTLD-CDR total scores compared to those with bvFTD. Using ROC curves, the new added domains had higher accuracy than the standard six CDR domains for detecting bvFTD. Logistic regression analyses showed that the language and behaviour domains independently enhanced the discriminative power between AD and FTD patients. Moreover, in ROC curve analysis, the FTLD-CDR outperformed the standard CDR in distinguishing bvFTD from AD.
Conclusion: Preliminary results show that the FTLD-CDR is a reliable tool in the diagnostic process of FTD, being able to clearly distinguish these patients from those with AD.
Disclosure: Nothing to disclose.

EPR-301

Motor and cognitive performance are associated beyond structural damage in relapsing-remitting multiple sclerosis

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Background and aims: Motor and cognitive dysfunctions are common in multiple sclerosis (MS). A deeper understanding of their relationship could highlight overlapping mechanisms of impairment. We assessed the association between motor and cognitive performance in a large group of MS patients, controlling for brain structural damage.

Methods: 86 healthy controls (HC) and 131 relapsing-remitting (RR) MS patients underwent a 3.0 T MRI and a functional examination including finger tapping test (FTT), nine-hole peg test (9-HPT) and 25-foot walk test (25-FWT). Clinical outcomes were converted to z-scores and analyzed according to the side of greatest motor impairment. Neuropsychological evaluation included Paced Auditory Serial Addition Test (PASAT-3") and Word List Generation (WLG), whose scores were corrected according to normative data. We computed partial correlations between motor and cognitive outcomes controlling for brain T2 lesion volumes (LV) and brain volumes.

Results: Compared to HC, RRMS patients had lower normalized brain volumes (NBV), grey matter volume (NGV) and deep GM volume (NDGV) ($p=0.007$) as well as worse performance in all motor tests ($p=0.008$). Mean PASAT-3" and WLG z-scores were -0.56 and -0.49. In RRMS, both motor and cognitive scores correlated with T2-LV, NBV, NGV and NDGV ($p=0.03$). After controlling for these MRI measures, significant correlation were found between neuropsychological and motor scores (FTT and 9-HPT) of the unimpaired side ($p<0.03$). No correlations were found between cognitive performance and 25-FWT or motor measures with the impaired side.

Conclusion: In RRMS patients, motor and cognitive performance are related beyond the effect of structural disease burden.

Disclosure: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

EPR-302

Lesion-symptom mapping of psychiatric symptoms in patients with acute ischemic stroke: a prospective cohort study

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Background and aims: Patients with acute ischemic stroke often suffer from post-stroke depression or anxiety. This may affect clinical outcome and cause higher mortality. So far, it is unknown if specific cerebral stroke lesions are more prone to lead to the development of such psychiatric conditions.

Methods: Our prospective cohort study included patients with acute ischemic stroke from July 2018 to May 2019. At baseline, each patient underwent an MRI for voxel-based lesion-symptom mapping with ITK-SNAP and MRIcron. To detect psychiatric disorders, we used the Mini-International Neuropsychiatric Interview (MINI), Beck Depression Inventory (BDI-II), Hamilton Rating Scale for Depression (HAM-D) and Spielberg's State-Trait Anxiety Inventory (STAI). A follow-up examination was performed within three to six months post-stroke.

Results: We included 98 patients. Mean age was 65.9 years, 56 patients (57.1%) were male, 67 patients (68.4%) completed follow-up. At baseline e.g., BDI-II showed 23 patients (23.5%) with pathologic scores indicating depression. Using non-parametric statistical mapping we found that these patients had a significant clustering of ischemic lesions in the putamen, temporal lobe and cerebellum. During follow-up 21 patients (31.1%) had pathologic BDI-II-Scores with strokes mainly located in the putamen and temporal lobe as well as in the parietal lobe, though in different areas compared to patients with initial conspicuous scores (as shown in Fig.1).

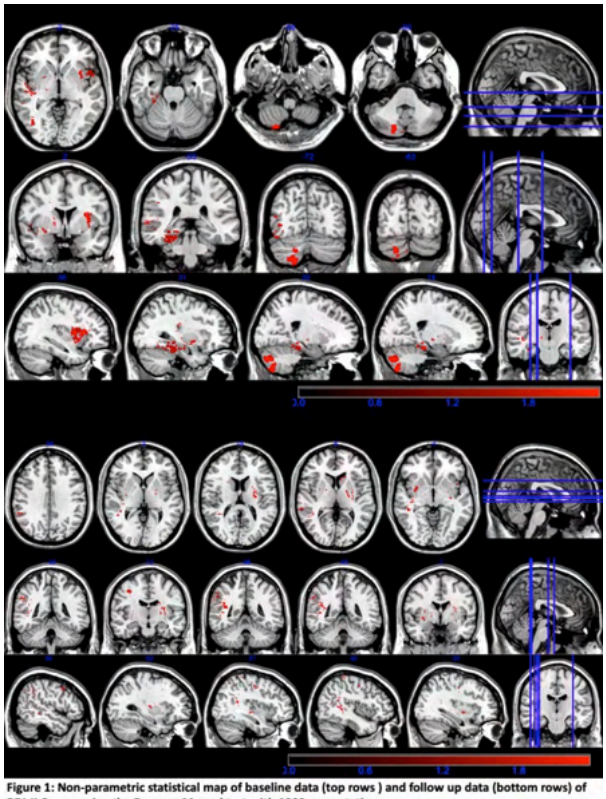

Figure 1: Non-parametric statistical map of baseline data (top rows) and follow up data (bottom rows) of BDI-II-Scores using the Brunner Munzel test with 1000 permutations.
The red scale indicates the z-score.

Beck Depression Inventory (BDI-II)

Conclusion: Our data suggest an association of ischemic lesions sites and subsequent development of psychiatric symptoms. Further research is needed to understand if these patients should be monitored more intensely and could benefit from early psychiatric treatment with better outcome or even lower mortality.
Disclosure: None of the authors have conflicts of interest or financial ties to disclose.

EPR-303

Clinical features and risk factors in recurrent transient global amnesia

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Background and aims: To define the demographic and clinical characteristics of patients with recurrent transient global amnesia (TGA) and to identify possible risk factors for recurrence.
Methods: Retrospective study of consecutive patients admitted to the Emergency Department requiring neurology consultation in a tertiary hospital during a period of 22 months (August 2018–May 2020) who met clinical criteria for TGA. A descriptive analysis and bivariate analysis were performed to identify risk factors for recurrence.
Results: A total of 124 patients with a diagnosis of TGA were included. 75 patients (60.5%) were women. The mean age was 65.18 years (SD±11.1) 23 patients had at least one recurrence. A higher incidence was observed in both groups in the early hours of the day (up to 44.3% of cases occurred between 8–12 am). There were no significant differences in the duration of the episodes or previous medical history (vascular risk factors, migraine, epilepsy or other pathologies). Female sex was the main risk factor for recurrence (p=0.018; OR 3.103; IC95% 1.123–8.575). n (35%) patients with recurrent TGA reported effort or Valsalva related maneuvers as a trigger (p=0.037).

	Isolated episode	Recurrent episodes	p-value
Patient number	101 (81,45%)	23 (18,55%)	
Age of onset (mean)	64,7±7.326	66,9±11.789	
Gender (w)	56 (55,44%)	19 (82,6%)	**0,018**

Table 1. Patient demographics

	Isolated episode	Recurrent episodes	p-value
Vascular risk factors	51 (50.49%)	14 (60.86%)	0,369
Hypertension	36 (35.64%)	10 (43.48%)	0,483
Diabetes mellitus type2	6 (5.94%)	0	0,592
Dyslipidaemia	34 (33.66%)	8 (34.78%)	0,918
Ischaemic heart disease	5 (4.95%)	0	0,583
Depression	2 (1.98%)	1 (4.35%)	1
Anxiety	2 (1.98%)	1 (4.35%)	1
Migraines	5 (4.95%)	0	0,583

Table 2. Patient comorbilities

Demographics, Episode characteristics

Conclusion: Female sex is associated with a higher risk of recurrence after TGA. Situations involving Valsalva related maneuvers are also significantly more frequent in recurrent TGA. We found no influence of other factors such as age, vascular risk factors or other possible triggers in TGA recurrence.
Disclosure: The author declares that he has no relevant or material financial interests that relate to the research described in this paper.

EPR-304

Longitudinal decline of visual short-term memory in ad and mci patients and relationship to hippocampal volume

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Background and aims: To assess whether a novel delayed reproduction Short-Term Memory (STM) binding task can longitudinally track memory decline in patients with Mild Cognitive Impairment (MCI) and Alzheimer's disease (AD) and investigate its relationship to baseline hippocampal volume.

Methods: 12 AD, 11 MCI patients plus 21 healthy elderly controls were recruited from the Oxford Centre for Cognitive Disorders. They performed the "What was where?" task on a tablet (where either one or three colorful shapes had to be identified and dragged to their original location after one or four seconds) and traditional neuropsychological tests at the 1st visit and after one year. They also underwent 3T MRI. The following metrics were calculated: Identification Accuracy (percentage of correctly identified items), Absolute Localization Error, Misbinding Rate (erroneously localizing an item to the remembered location of another item in memory), Guessing and Target detection rates, memory Imprecison (as a continuous measure), Identification and Localization Time.

Results: MCI and AD patients showed lower identification accuracy, higher absolute localization errors, higher misbinding and guessing rates, fewer targets detected, longer times to correctly identify and localize the items and higher memory imprecision, which increased with time (Figure 1). These metrics correlated with standard memory tests as ACE and DS and baseline hippocampal volume (Figure 1).

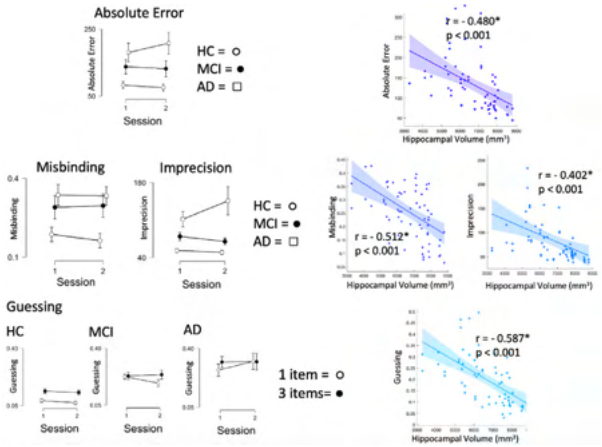

Figure 1: Longitudinal decline of "What was where?" Short-Term Memory task metrics and relationship with baseline hippocampal atrophy.

Conclusion: Visual STM decline could be tracked by novel digitized metrics that reflect baseline hippocampal atrophy. This task might be a useful marker of memory decline and hippocampal dysfunction in the earliest stages of AD.

Disclosure: Nothing to disclose.

Epilepsy 4

EPR-305

Investigating the impact of anterior temporal lobe resection on reading networks in patients with temporal lobe epilepsy

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Background and aims: Anterior temporal lobe resection (ATLR) is an effective treatment option in patients with intractable temporal lobe epilepsy (TLE) but may be complicated by postoperative language impairment. We used functional magnetic resonance imaging (fMRI) to study neural correlates of reading in TLE patients before and after ATLR.
Methods: We studied 44 patients with TLE due to hippocampal sclerosis (24 left) and 18 healthy controls. All patients performed a reading task preoperatively and four months following ATLR. Preprocessing and analysis were performed with statistical parametric mapping employing a general linear model. We evaluated group specific task activations in TLE patients and healthy controls, and pre- and postoperative differences for left and right TLE (lTLE, rTLE) individually.
Results: In controls, greater left than right activations in the superior temporal gyrus (STG), the middle temporal gyrus (MTG), and the left hippocampus and inferior frontal gyrus (IFG) were observed. Preoperatively, lTLE showed left lateralized activations in the MTG, IFG and only left-sided hippocampal activations. In rTLE, bilateral activations were seen in the MTG whereas only left-sided activations were detected in the IFG and hippocampus. Postoperatively, lTLE showed bilateral activations in the MTG and additional right hippocampal activations. In rTLE, only left-sided activations were seen in the MTG, STG, IFG and hippocampus following ATLR.
Conclusion: Reading sentences involved predominantly left frontal and temporal areas, including the hippocampus, in controls and patients with left and right TLE preoperatively. LTLE patients tend to recruit areas within the right hemisphere following ATLR, highlighting the importance of contralateral language networks supporting reading function.
Disclosure: Nothing to disclose.

EPR-306

Atherosclerotic risk and antiepileptic drugs: preliminary results of the ELVIS study

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Background and aims: Most epileptic patients require chronic use of antiepileptic drugs (AED), which have been associated with increased risk of atherosclerosis. The advent of a newer-generation of AED may reduce this risk. Our aim is to analyse the atherosclerotic risk of enzyme-inducing antiepileptic drugs (EIAEDs) versus non-EIAEDs (NEIAEDs).
Methods: We present the preliminary results of a 1-year prospective longitudinal study. Patients were divided in two groups based on their antiepileptic treatment: EIAEDs (such carbamazepine) and NEIAEDs (such levetiracetam). Clinical data, blood analysis results and ultrasonographic measures (carotid artery intima-media thickness [CA-IMT] and atherosclerotic plaques) were collected. CA-IMT was measured according to Manhein Consensus. Descriptive and inferential statistics were employed.
Results: 22 patients (eleven patients in each group) were included, 54.5% female, with a mean age of 45.14 (±12.02) years old. There were no differences in the mean duration (years) of the AED treatment between groups (4.75±3.78 vs 3.18±3.27, $p>0.05$). In patients with EIAEDs, the mean CA-IMT (0.63±0.11 mm vs 0.54±0.56mm, $p<0.05$) and the prevalence of atherosclerotic plaques (54.6% vs 0.0%, $p<0.05$) was significantly higher than in NEIAEDs. On multivariate analysis, the antiepileptic treatment was not an independent predictor of CA-IMT (OR 0.79; 95% CI: 0.87–1.04, $p=0.30$).
Conclusion: These preliminary results suggest that patients under EIAEDs could have a higher atherosclerotic risk. However, the antiepileptic treatment may not be the main explanatory factor, age or classic vascular risk factors having a greater role. This association requires further investigation, along with the ongoing study.
Disclosure: The project has received research grants from Bial.

EPR-307

Cenobamate as adjunctive therapy in adults with uncontrolled focal seizures: time to onset of efficacy during titration

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Background and aims: Cenobamate is a new antiseizure medication (ASM) approved in the US for uncontrolled focal (partial-onset) seizures in adults. Two international, double-blind, placebo-controlled trials (C013/C017) demonstrated cenobamate efficacy and safety. Here we report time to onset of efficacy during titration of cenobamate in these studies.

Methods: Adults with uncontrolled focal seizures and taking 1–3 concomitant ASMs were enrolled in Study C013 and C017. Concomitant ASM changes were not allowed during the double-blind period. Time to onset of efficacy in patients receiving cenobamate versus placebo was evaluated during the six weeks of cenobamate titration (Table 1). Post-hoc analysis of efficacy examined the percent reduction in seizure frequency from baseline to each week during titration using a Wilcoxon rank-sum test (C013) or an ANCOVA model fit to the ranked values of baseline seizure rate and treatment group (C017).

Results: Patients receiving cenobamate had significant reductions in median percent seizure frequency versus placebo starting from the 1st 1–2 weeks of cenobamate titration at the initial dose of 50mg/day (C013: -26.7% cenobamate vs -15.1% placebo, p<0.05, Figure 1; C017: -36.4% cenobamate vs -20.0% placebo, p<0.05, Figure 2). Sustained significant decreases in seizure frequency versus placebo were seen throughout the 6-week titration in both studies. The median reduction in seizure frequency was progressively higher with increasing cenobamate doses of 100, 200, and 400mg/day (Figure 2).

Conclusion: Onset of cenobamate efficacy in significantly reducing seizure frequency occurs early and at lower doses than the target dose for maintenance therapy and it improves at higher doses.

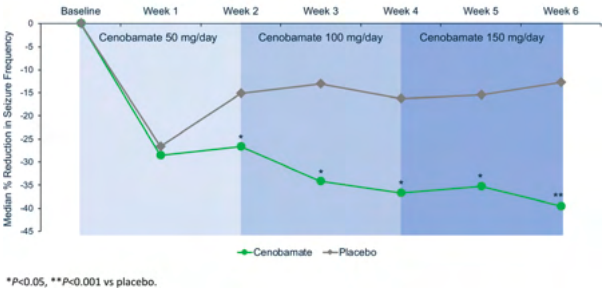
Table 1. Cenobamate titration in study C013 and C017 (double-blind period).

	C013	C017
Cenobamate target dosages	200 mg/day	100 mg/day 200 mg/day 400 mg/day
Titration phase, weeks	6	6
Maintenance phase, weeks	6	12
Titration schedule	Starting dose of cenobamate 50 mg/day and increased 50 mg/week every 2 weeks until reaching the target dose of 200 mg/day.	Starting dose of cenobamate 50 mg/day and increased 50 mg/week, until reaching the target dose of 100 or 200 mg/day. For patients randomly assigned to the 400 mg/day dose group, once the 200 mg/day dose was reached, the dose was up-titrated by 100 mg/day per week to the target dose.[a]

[a]The initial starting dose of the original faster C017 titration schedule was 100 mg/day with weekly increments of 100 mg/day to the target-dose (completed by 46/437 patients [10.5%]). The amended titration schedule reduced the initial starting dose to 50 mg/day and slowed the titration rate to the target dose to improve tolerability.

Table 1.

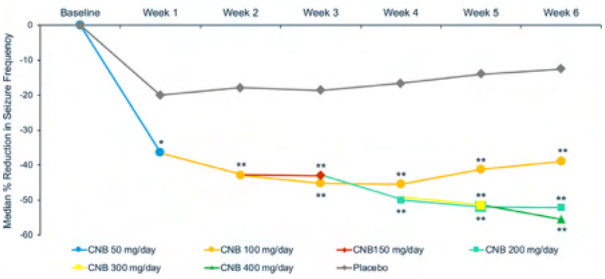
Figure 1. Time to onset of efficacy during titration in study C013.



*P<0.05, **P<0.001 vs placebo.

Figure 1.

Figure 2. Time to onset of efficacy during titration in study C017.



Patients are grouped by the cenobamate dose received at each week of titration.*P<0.05, **P<0.001 vs placebo. CNB, cenobamate.

Figure 2.

Disclosure: Studies C017 (NCT01866111) and C013 (NCT01397968) were sponsored by SK Life Science, Inc. (Paramus, NJ, USA) and these analyses were supported by Arvelle Therapeutics International GmbH (Zug, Switzerland).

EPR-308

Refractory opercular myoclonic-anarthric status epilepticus in coexistence with ANTI- SOX1 antibodies

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Background and aims: Opercular myoclonic-anarthric status epilepticus (OMASE) as a clinical phenotype of new onset refractory status epilepticus (NORSE) is an uncommon disorder. OMASE is characterized by fluctuating cortical dysarthria associated with epileptic myoclonus involving glossopharyngeal musculature. AntiSOX1 antibodies have rarely been identified in cases of NORSE.
Methods: To present a patient with refractory OMASE in coexistence with antiSOX1 antibodies.
Results: A 74-year-old female patient was admitted to the ED due to possible complex partial seizures with clonic rhythmic movements of the angle of the mouth, tongue and right arm distally. Upon examination severe dysarthria was presented. Brain MRI showed atrophy at the area of the left Sylvian fissure. EEG showed slow waves at the left frontotemporal area. Interictal brain SPECT revealed reduced blood flow at the right temporal lobe and the right thalamus. Autoimmune screen panel results showed positive SOX-1 autoantibodies. CT chest/abdomen and mammogram revealed non specific findings for malignancy. A whole body positron emission tomography was recommended. A variable combination of antiepileptic drugs including lacosamide,phenytoin and finally perampanel was administered with partial response. Five day course of methylprednisolone was administered resulting in improvement of speech and swallowing and of the partial motor clonic movements.
Conclusion: OMASE as a clinical phenotype of NORSE is a rare neurological disorder Screening for possible autoimmune etiology is important in order to provide accurate diagnosis and the appropriate therapeutic plan.
Disclosure: Nothing to disclose.

EPR-309

Long term outcome after a 1st seizure in an adult population

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Background and aims: Approximately 8% to 10% of the population will experience a seizure during lifetime. On the contrary, just a small percentage of patients finally develops epilepsy. A diagnosis of epilepsy has medical, social and emotional consequences. We aimed to classify the different clinical characteristics of a group of patients with a 1st epileptic seizure and to determine either the risk of long-term recurrence or the mortality.
Methods: We analyzed a group of adult patients (>14 years old) admitted to the emergency room for a 1st, epileptic seizure between January the 1st 2006 and December 31st 2009. In the setting of a retrospective, single-center, longitudinal cohort study, 233 patients were evaluated with a long-term follow-up (maximum of 14 years).
Results: Among the 233 patients, 174 (75%) had an unprovoked seizure, while 59 (25%), had a provoked seizure. At follow-up, 96 patients had seizure recurrence, 51% within the 1st year of follow-up. No differences of recurrence were found between patients that started anti-seizures treatment immediately after the 1st seizure and those in which the treatment was delayed (p=0.204). A diagnosis of epilepsy was eventually made for 85% of patients with a first unprovoked seizure and 21% with a 1st provoked seizure (p=0.001). In terms of mortality, no difference was observed comparing provoked and unprovoked seizure groups.
Conclusion: The recurrence 'risk was not modified by the immediate start of antiepileptic treatment. The etiology of a first seizure, was the most important seizure recurrence risk factor.
Disclosure: I have no discosure.

EPR-310

Comparative efficacy and safety of anti-epileptic drugs in paediatric populations: A network meta-analysis

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Background and aims: Several randomized placebo-controlled trials assessed the clinical efficacy and safety of perampanel in paediatric and mixed-age population epilepsy. As no trials included active treatment comparators, we conducted a network meta-analysis (NMA) to assess the relative efficacy and safety of perampanel versus 3rd-generation anti-epileptic drugs (AEDs) approved for epilepsy treatment in paediatric populations.
Methods: A systematic literature review identified NMA eligible studies. Endpoints of >50%, >75% and 100% seizure reduction, drug-related adverse events (AEs), and treatment discontinuation due to AEs were extracted. Bayesian NMA was performed, considering dose-pooled (DPA) and dose-stratified analyses (DSA).
Results: We identified 15 eligible studies. In DSA, perampanel 8mg/d was as effective as brivaracetam 100mg/d (relative risk [RR]: 0.97; 95% credible interval [CrI]: 0.75–1.28), lacosamide 300mg/d (RR: 1.11; CrI: 0.78–1.66) and pregabalin 300mg/d (RR: 0.78; CrI: 0.58–1.14) and more effective than eslicarbazepine 200mg/d (RR: 1.66; CrI: 1.06, 2.85) in achieving 50% seizure reduction. For 75% seizure reduction, brivaracetam 8mg/d was similar to lacosamide (RR: 1.01; CrI: 0.61–1.73) and more effective than eslicarbazepine (RR: 2.07; CrI:1.09–4.16). Only perampanel 8mg/d and brivaracetam 100mg/d reached significant differences in seizure freedom versus placebo; the RRs (CrIs) of seizure freedom for perampanel 8mg/d versus brivaracetam 100mg/d, brivaracetam 150mg/d, eslicarbazepine 200mg/d and lacosamide 300mg/d were 0.5 (0.13–1.95), 1.56 (0.11–13.75), 2.09 (0.38–11.32) and 2.16 (0.73–6.72), respectively. No differences were observed between AEDs in DPA and in safety outcomes.
Conclusion: Perampanel has similar efficacy and safety as other third-generation AEDs and greater 50% and 75% seizure reduction rates than eslicarbazepine, at medium doses.
Disclosure: Eisai Inc. was the funding source and was involved with all stages of the study conduct and analysis.

EPR-311

Preliminary experience using a minimally invasive sub-scalp device for ultra-long term seizure monitoring

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Background and aims: Accurate identification of seizure activity has important clinical implications. Unrecognised seizure activity presents significant challenges to patient management. Implantable device studies have shown the potential of such systems but have been relatively invasive. We conducted a preliminary study of a minimally invasive sub-scalp device to continuously record EEG to detect seizures from a variety of anatomical locations.
Methods: Eight patients with refractory epilepsy with at least one seizure weekly have been implanted with sub scalp devices (Minder), with four electrode contacts deployed in a coronal plane posterior to vertex providing two channels of data. Data is continuously captured via a behind-ear unit and transferred wirelessly to a mobile phone, from where it is accessible remotely via the cloud. Recordings were compared to a one week inpatient video-EEG monitoring session for four of these subjects. EEG recordings from both systems were reviewed blindly by two neurologists. The study was conducted as part of a registered clinical trial.
Results: The procedures were well tolerated, no significant complications occurred. The sub scalp recording captured all 31 events identified during the video-EEG period from the four subjects. Two events were initially identified on the sub scalp monitoring system alone. Of the 20 total patient reported events, 12 were not associated with clinical or EEG changes on either system.
Conclusion: A sub-scalp system can capture continuous EEG data and accurately detect focal seizure activity. Significant disparities between reported and confirmed seizure activity were found. Sub-scalp systems could potentially provide considerable clinical utility.
Disclosure: Some of the authors declare that they have personal financial interests.

Neuroimaging 2

EPR-312

Head ct scans for syncope in the emergency department

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Background and aims: Head CT is often routinely performed in emergency department (ED) patients with syncope, yet few studies assessed its value. Our aim was to determine the yield of head CT in ED patients with syncope and analyze the factors associated with a pathologic CT.
Methods: A retrospective review of consecutive patients who were admitted to the ED due to syncope or loss of consciousness from January 2018 through September 2019. Demographic and clinical data were extracted from the electronic medical records and brain imaging were reviewed.
Results: 3,984 patients were admitted to the ED in the designed period. 442 were younger than 18. The oldest patient in the cohort was 101 years old. 44% were males and 56% females. 49% were admitted for further evaluation. 27.53% of the patients underwent head CT scans. The reasons for obtaining imaging included trauma of the head or face, focal neurological deficits, suspected seizure, confusion, altered mental status, headaches, fever, vomiting or use of anti-coagulation. Only 7.29% of the head CT scans were pathologic. 37.5% demonstrated past pathologies such as infarcts or brain hemorrhage. 22.5% demonstrated new hemorrhage, 12.5% revealed face of skull fractures. Two revealed signs of acute stroke and five revealed space occupying lesions.
Conclusion: This study suggest the need to reduce the use of head CT in patients presenting to the ED with syncope. Developing a simple scoring algorithm utilizing clinical risk factors could help predict the non-trauma patients who will benefit from CT imaging, resulting in reduced radiation exposure without sacrificing sensitivity.
Disclosure: Nothing to disclose.

EPR-313

Limbic System Nuclei Morphometry in Substance Dependence

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Background and aims: Level of neurodegeneration could help to objectify the severity of dependence and clear the pathophysiological mechanisms of addiction. Moreover, the functional and morphological outcome of drug withdrawal is also under discussion. We aimed to analyze the volume in the main subcortical nuclei of the limbic system among substance users.
Methods: 204 individuals went under the MRI, from whom 31 were with actual opioid dependence syndrome, 50 individuals with alcohol dependence syndrome, 62 with opioid drug withdrawal for more than five years (ICD-10), and 61 age- and sex-matched healthy controls. Voxel-based morphometry of 25 thalamic, nine amygdalas and 19 hippocampal nuclei bilaterally was performed using FreeSurfer 6.0. ANOVA and Levene's tests with Bonferroni correction were used for statistical analysis in SPSSStatistics 25.0.
Results: All groups of substance users showed a smaller volume of amygdala nuclei from right side predominantly compared to healthy controls, but the withdrawal group in a less degree. Hippocampal grey matter decreasing was predominantly identified among active drug addicts, also in alcohol dependence and withdrawal groups too, compared to healthy controls. The decreased grey matter was identified in thalamic nuclei in active addicts, whereas the size of right thalamic nuclei in the withdrawal group was increased compared to healthy controls.
Conclusion: 1) Decreased grey matter volume in nuclei of main subcortical limbic structures could represent the existence of substance dependence; 2) Drug withdrawal characterised by a partially increased right thalamus volume. Future researches are needed to understand the cause of this phenomenon.
Disclosure: No relationships to disclose.

EPR-314

Chronic active MRI lesions in progressive multiple sclerosis patients undergoing ocrelizumab treatment

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Background and aims: In multiple sclerosis (MS), paramagnetic rim lesions (PRL) generally expand over time and are associated with a more aggressive disease course. Here we analyzed PRL on scans obtained before and after starting the disease-modifying-treatment (DMT) ocrelizumab in progressive MS patients (PMS).

Methods: 12 PMS underwent 3T MRI before and at a median time of 13 months (range 6–18) after starting ocrelizumab. A 3D-EPI sequence allowing PRL assessment on phase images and Quantitative Susceptibility Mapping (QSM) analysis was acquired. PRL and comparable non-PRL control lesions were classified into "shrinking," "steady," or "expanding" based on their adjusted log-volume percentage change over time (-1, -1–1 and 1, respectively).

Results: Of 12 participants, 11 had at least one PRL; a total of 54 PRL were identified by consensus. No PRL disappeared at follow up (Figure) and no mean lesion QSM susceptibility or volume changes were measured in PRL areas before and after ocrelizumab administration (6,7 and 8,4 ppb, p=0.6; 592 and 602mm3, p=0.9). After ocrelizumab administration, longitudinal volume changes were not significantly different in PRL vs non-PRL control lesions (steady/expanding vs. shrinking; p=0.3).

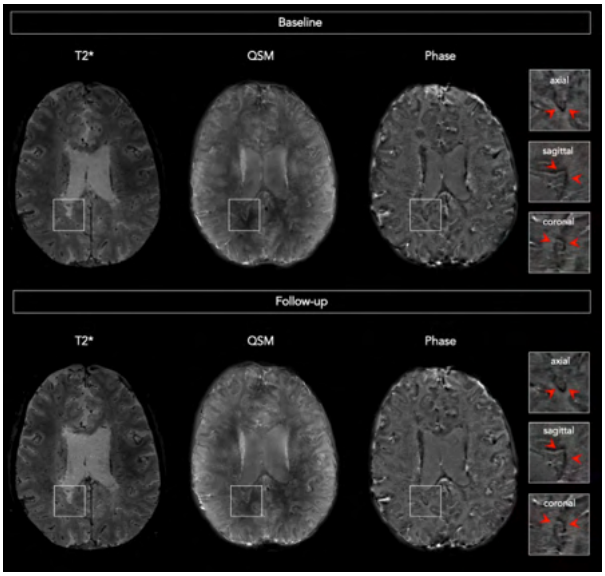

Figure. Representative susceptibility based T2*-magnitude, QSM and phase images from one primary progressive multiple sclerosis patient showing the same PRL (magnified view) at pre-ocrelizumab baseline and at the 14 month post-ocrelizumab follow-up.

Conclusion: No qualitative or quantitative susceptibility changes were found pre- and post-ocrelizumab administration consistent with the notion that PRL are not the primary target of available DMT. However, considering that PRL have been shown to expand over time, the fact that PRL volumes did not change compared to non-PRL, warrants additional study in a larger cohort with longer post-DMT follow-up and comparator DMT.

Disclosure: Nothing to disclose.

EPR-315

Atrophy quantification in multiple sclerosis: application to the multicenter INNI dataset

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Background and aims: Aim of this study was to compare a set of state-of-art methods for gray matter (GM) and whole-brain atrophy measurements on the Italian Neuroimaging Network Initiative (INNI) dataset, where MRI and clinical data from multiple sclerosis (MS) patients and healthy controls (HC) are collected by Italian Research Centers with internationally recognized expertise.

Methods: SIENAX, SPM-v12 and Jim8 (Xinapse Systems) software were selected. 3D MPRAGE from 457 MS and 271 HC were collected from INNI repository. For cross-sectional GM and whole-brain atrophy measures, we evaluated the agreement and correlation among the results of the pipelines. Moreover, the capability of the software in discriminating between HC and MS was assessed. A bias due to the different acquisition Center and the sample size requirement were also evaluated.

Results: We found significant agreement ($p<0.05$) among the software: the highest between the results of SPM and Jim8 (0.91, $p<0.05$) and the lowest between SIENAX and Jim8 (0.6, $p<0.05$), for both GM and whole-brain (Figure 1). Comparing distributions, SIENAX for GM volumes and Jim8 for brain volumes better separated HC from MS ($p<0.05$). None of the pipeline showed a bias in respect to a particular Center.

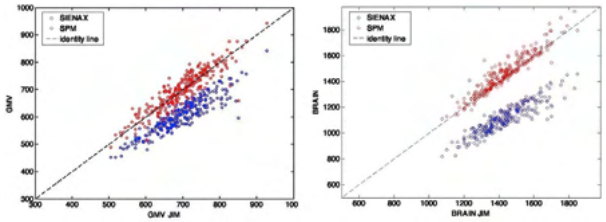

Figure 1: On the left, the scatter plot for the comparisons of GM volume results (in ml) on HC for the different software. On the right, the scatter plot for the comparisons of whole brain volume results (in ml) on HC for the different software.

Conclusion: Using the INNI dataset, we found an acceptable agreement among the software. The free-licence (SIENAX), the speed and the facility of integration in the clinical routine (Jim8, SIENAX) are noteworthy for the selection of the atrophy pipeline. To move those atrophy tools from the research setting to the clinical practice, normative data from at least 150 HC should be available.

Disclosure: This project has been supported by a research grant from the Fondazione Italiana Sclerosi Multipla (FISM2019/S/3), and financed or co-financed with the '5 per mille' public funding.

EPR-316

Assessment of white matter atrophy in multiple sclerosis using advanced diffusion weighted imaging models

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Background and aims: In this study, we assessed white matter (WM) atrophy in multiple sclerosis (MS) both cross-sectionally and longitudinally with advanced DWI techniques and explored whether these advanced measures would better explain clinical disability in comparison with the conventionally used metrics.

Methods: Baseline and 1-year clinical evaluation and 3D T1-weighted and a multi-shell DWI sequence were obtained from 86 MS patients and 55 healthy controls (HC). Maps of fractional anisotropy (FA) and mean diffusivity were derived from DWI; intra-cellular volume maps were computed from neurite orientation dispersion and density imaging model. A fixel-based morphometry analysis was applied to estimate voxel-wise fiber bundle cross-section (FC) atrophy in MS compared to HC.

Results: Only FC measure showed a significant atrophy in relapsing-remitting (RR) MS compared to HC and in secondary progressive compared to RRMS patients, mainly located in the cortico-spinal tract, splenium of the corpus callosum, optic radiation and the cingulum (p-value<0.05, Figure 1), both at baseline and after one year. Globally, only FA and FC showed a significant correlation with the Expanded Disability Status Scale (EDSS), both at baseline (r=-0.55) and follow-up (r=-0.4).

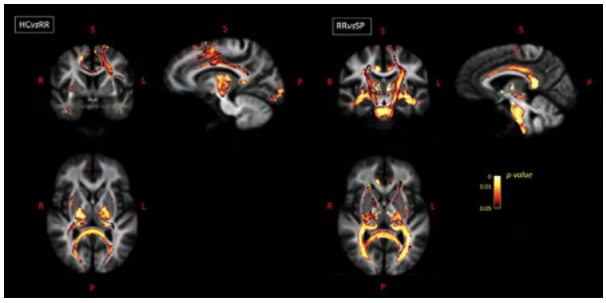

Fig 1: Baseline visit. Left, fibers with significantly decreased FC in RRMS patients than HC are shown, with fixels colored by FWE-corrected p-value. Right, fibers with significantly decreased FC in SP compared to RRMS patients are shown.

Conclusion: By identifying tract-specific differences, voxel-based analyses clearly confirmed the ability of the FC measure to detect WM atrophy with greater anatomical specificity compared to other measures and better capability to distinguish MS clinical phenotypes. In the assessment of longitudinal variations, only FC was able to reveal a significant WM degeneration in MS patients compared to HC, which contributed to explain clinical disability.

Disclosure: This study has been partially supported by FISM–Fondazione Italiana Sclerosi Multipla–cod. 2018/R/16 and financed or cofinanced with the "5 per mille" public funding.

EPR-317

A study on GLUCEST in the brain of patients with acute carbon monoxide poisoning

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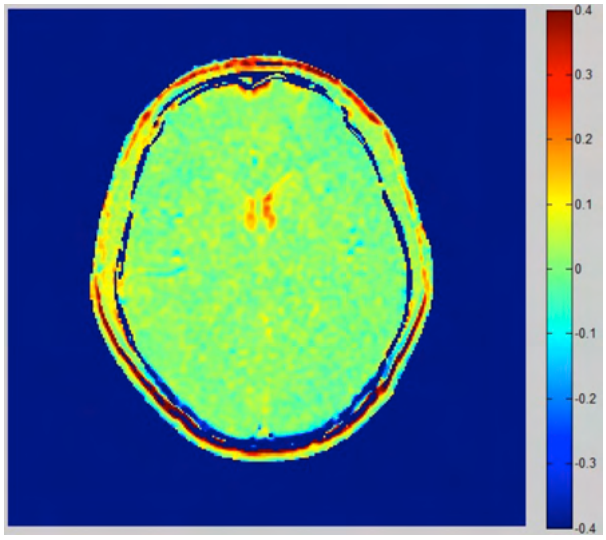
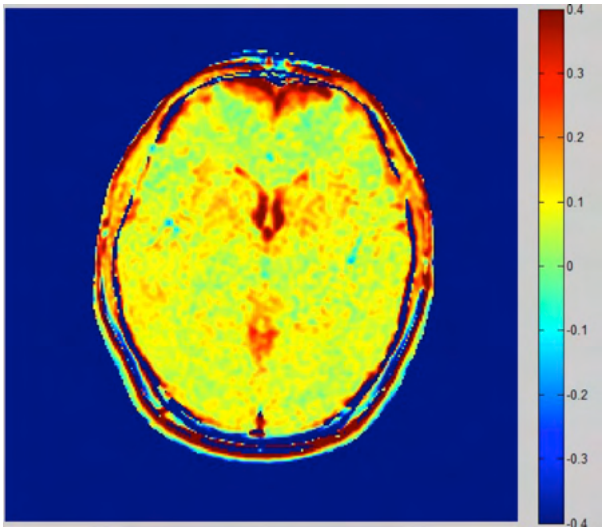
Background and aims: To evaluate the diagnostic and prognostic values of glutamate weighted chemical exchange saturation transfer (GluCEST) magnetic resonance imaging as a quantitative method on acute carbon monoxide poisoning.

Methods: 20 patients with diagnosis of acute carbon monoxide poisoning encephalopathy (3±1.25 days after poisoning) and 10 healthy subjects were examined with conventional magnetic resonance imaging Glucest scan. Patients were divided into two groups according different clinical outcome.

Results: The maps of Glucest showed the concentration of glutamate (Glu) in bilateral hippocampustemporal cortex and globus pallidus exposed to carbon monoxide was higher than that of controls ($p<0.05$). Patients in poor outcome group had higher concentration of glutamate (Glu) in globus pallidusthan that in good outcome group.



GLUECEST maps of healthy control



GLUECEST maps of patient with acute carbon monoxide poisoning

Conclusion: Magnetic resonance Glu-CESTcan monitor the change of glutamate content in vivo brain noninvasively. It provides a new imaging study for the assessment of acute brain injury caused by carbon monoxide poisoning. A higher GLUECEST %-value of the lesion in early stage may strongly suggest the poor prognosis of carbon monoxide poisoning.

Disclosure: This study were Grant for Key Disciplinary Project of Clinical Medicine under the Guangdong High-level University Development Program, China; Clinical teaching reform project in Guangdong Province China (2018 JD058).

Neurological manifestation of systemic diseases

EPR-318

Eosinophilic fasciitis: a most unusual presentation

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Background and aims: Eosinophilic fasciitis (EF) is a skin and soft tissue disorder manifesting as painful edema followed by progressive skin thickening and joint contractures. On the initial phases, peripheral blood eosinophilia and hypergammaglobulinemia can also be found. Of unknown etiology and pathophysiology, the disorder is rare and probably underdiagnosed.
Methods: Case report from a tertiary care hospital.
Results: A 76-year-old male was referred for evaluation of a probable akinetic-rigid syndrome of two years of evolution. He described progressive myalgia, skin changes and joint contractures with reduced mobility. The exam showed thickened and atrophic skin (Peau d'orange), "groove sign" (Figure1) and decreased range of motion of temporomandibular, elbow, knee and ankle joints. On neurological examination, strength was normal, ankle jerks were absent and mildly reduced pinprick sensation and vibration sense distally in the lower limbs. Laboratory tests revealed hypergammaglobulinemia and CRP elevation. Nerve conduction studies demonstrated an axonal sensorimotor polyneuropathy (Figure2). Lower limbs MRI showed diffuse muscular edema (Figure3). Both autoimmune and heavy metals panels were negative. Skin biopsy showed dermal infiltration by CD8+T-cells and eosinophils. Muscle biopsy was consistent with an inflammatory myopathy with perymisial CD8+T-cells and eosinophilic infiltrates. After mild response to prednisone and IVIG, methotrexate was initiated with clinical stabilization. Temporomandibular joint contracture was treated with botulinum toxin injections.

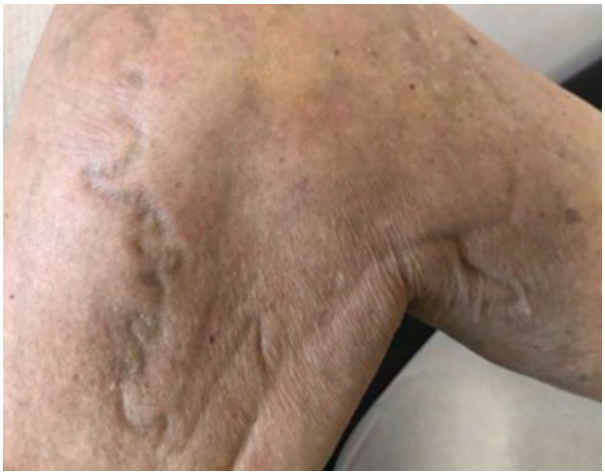

Figure 1. Peau d'orange and groove sign in leg. Decreased range of flexoextension of knee.

	CMAP, mV	MCV, m.s^{-1}	DML, ms	SNAP, µV	SCV, m.s^{-1}	F wave, ms
Radial N.	-	-	-	18	58.8	-
Median N.	5.1	50.5	4.3	16.8	45.2	30.9
Ulnar N.	4.7	51.4	3.3	23.9	56	30.4
Tibial N.	0.7	37.1	7.4	NR	-	51.4
Peroneal N.	0.3	38	7.2	NR	-	NR

CMAP = compound motor action potential; DML = Distal motor latency ; F wave = minimum latency of F wave; SNAP = sensory nerve action potential; MCV = Motor conduction velocity; SCV = sensory conduction velocity .

Figure 2. Initial nerve conduction study.

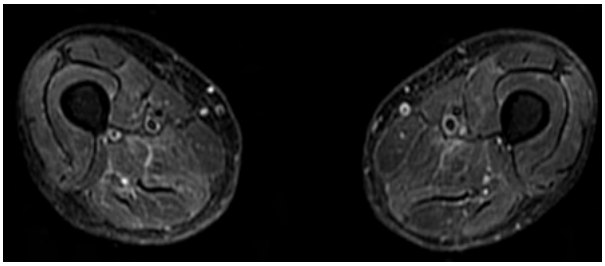

Figure 3. Lower limbs muscular MRI (T2 STIR). Diffuse muscular edema, predominant in posterior compartment.

Conclusion: We report a neuromuscular presentation (inflammatory myopathy and polyneuropathy) of EF, in addition to cutaneous and articular features. This association of myopathy and polyneuropathy is highly unusual. This, together with the rarity of the disease, may have contributed to a diagnostic delay.
Disclosure: Nothing to disclose.

EPR-319

Extensive leukoencephalopathy in Coeliac disease

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Background and aims: Coeliac disease (CD) is an autoimmune enteropathy caused by gluten exposure in genetically predisposed individuals. CD can be occasionally associated with a varying burden of brain white matter (WM) lesions with or without central neurological manifestations (e.g., epilepsy, cerebellar ataxia, and headache), and subcortical occipital calcifications.
Methods: We reviewed the clinical and neuroimaging features of three females with a late diagnosis of CD (4^{th} or 5^{th} decade) assessed at our Adult Leukodystrophy Outpatient Clinic because of an extensive leukoencephalopathy considered of unknown origin.
Results: The three patients (46-, 57- and 68-year-old, respectively) presented different neurological manifestations (i.e., progressive cerebellar ataxia, chronic headache, and chronic headache lately complicated by a rapidly progressive motor neuron disease), but exhibited a comparable brain MRI pattern consisting of multifocal/confluent T2-FLAIR supratentorial WM hyperintensities with prominent lobar distribution and relative sparing of periventricular and subcortical regions. Occipital calcifications were present in one case. A comprehensive diagnostic work-up excluded other causes of WM diseases.
Conclusion: Clinicians should be aware that, in patients with CD, the detection of an extensive leukoencephalopathy on neuroimaging should be primarily considered as a CD manifestation, especially when the WM changes have a prominent lobar distribution and lack of definite clinical correlations. This conclusion is in agreement with few previously reported observations. The extension of WM changes might be caused by a long duration of gluten exposure prior to CD diagnosis, while their distribution appears to be more compatible with a microangiopathic process than a demyelinating one.
Disclosure: The authors declare no conflict of interest.

EPR-320

Characteristics of Patients With p.V50M and p.T80A Mutations Associated With Hereditary Transthyretin Amyloidosis

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Background and aims: Hereditary transthyretin amyloidosis (hATTR or ATTRv [variant]) is a progressive, fatal disease caused by mutations in the transthyretin gene (TTR) that result in multisystem dysfunction, including polyneuropathy and cardiomyopathy. The p.V50M and p.T80A mutations are among the most common TTR mutations in European patients.
Methods: This analysis utilised data from patients enrolled in hATTR Compass, a genetic testing programme offered in the United States and Canada for patients suspected of having hATTR with polyneuropathy or a family history of hATTR. Next-generation sequencing was performed using gene panels for neuromuscular and cardiac disorders.
Results: Of 79 patients studied, 37 had the p.V50M mutation and 42 had the p.T80A mutation. The average age at testing for p.V50M and p.T80A patients was 56 and 52 years, respectively; white ethnicity was the most common (77% for p.V50M and 100% for p.T80A). Of the p.V50M and p.T80A patients in the genetic testing programme, cardiologists referred 27% and 33% and neurologists referred 38% and 26%, respectively. Common symptoms/manifestations for the p.V50M and p.T80A patients included heart disease (50% and 65%); bilateral carpal tunnel syndrome (15% and 35%); and sensory (70% and 65%), motor (40% and 30%), and autonomic dysfunction (40% and 30%).
Conclusion: Diagnosis of hATTR is challenging because it can present similarly to other diseases, but hATTR commonly presents with both polyneuropathy and cardiomyopathy. It is critical that clinicians recognise symptoms of hATTR and refer patients for genetic testing to facilitate diagnosis and initiate disease-modifying therapy for this fatal disease.
Disclosure: Funding was provided by Akcea Therapeutics, an Ionis Company; editorial assistance was provided by ApotheCom and scientific support was provided by Ambry Genetics.

EPR-321

Bilateral functional popliteal artery entrapment syndrome as a cause of recurrent falls while running: A case report

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Background and aims: Functional popliteal artery entrapment syndrome (PAES) is an underdiagnosed clinical entity affecting mainly young athletic males and military personnel. It presents with exertional claudication from pressure to the vascular walls by adjacent myofascial structures.
Methods: We present an atypical case of bilateral functional PAES in a young woman.
Results: An 18-year-old woman with free past medical history was referred for neurological evaluation due to recurrent falls and transient painless weakness while running. Her neurological examination, electromyography and laboratory workup were normal. A forearm exercise test measuring lactate and ammonia was also normal. Symptoms were reproduced after approximately three minutes of intense running on a treadmill. Electrolytes and muscle enzymes before and after running were normal. An arterial ultrasound of the lower limbs revealed normal doppler artery soundwaves. However, upon performing plantar flexion and dorsiflexion of the feet, a decrease in flow velocity was noted bilaterally. Vascular surgeons were consulted and Magnetic Resonance Imaging and Angiography of the popliteal fossae in functional positions revealed severe pressure phenomena on the popliteal arteries between the plantaris and popliteus muscles. The ankle-brachial index was normal in neutral position, but dropped by 0,45 on plantar flexion, confirming a diagnosis of functional PAES. Conservative treatment was suggested due to the functional nature and longterm prognosis of the disease.
Conclusion: Functional PAES should be included in the differential diagnosis of exertional lower limb weakness in young patients, even in the absence of pain. Special tests in neutral and functional positions of the limbs are warranted to ensure diagnosis.
Disclosure: Nothing to disclose..

EPR-322

Acute chorea and masked polycythaemia vera

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Background and aims: Late onset chorea poses a challenging diagnosis with a broad differential diagnosis with polycythaemia vera usually presenting with characteristic laboratory values.
Methods: Clinical case
Results: We present a case of a 83-years-old woman with a personal history of anal canal tumour treated with chemo-radiotherapy eight years ago, valvular cardiopathy, arterial hypertension, type 2 diabetes mellitus and dyslipidaemia. Presented with a 2-month clinical picture of involuntary movements described by the family as "fidgety" movements that started abruptly. This movements were generalized, broad, continuous and provoked social embarrassment, balance disturbances and painful oral ulcers. The patient had no known family history of neurology disorders. Diet was normal and no new medications were introduced recently. Comorbidities were controlled. The neurological exam revealed a generalized chorea predominantly involving facial and tongue muscles as well as distal muscles of upper and lower limbs. Gait was normal except for the movement disorder interference. The remaining neurologic exam was unremarkable. Blood work revealed persisting leucocytosis and thrombocytosis and low EPO. MRI imaging revealed marked vascular leukoencephalopathy. Body CT scan (thoracic, abdominal and pelvic) showed a slight splenomegaly. Electroencephalogram and LP were normal. Genetic testing for V617F mutation was positive. Hydroxyurea and acetylsalicylic acid were started and a presumed diagnosis of polycythaemia vera was made, despite no polyglobulia.
Conclusion: Regular blood tests should be part of the routine follow-up of patients with late onset chorea with genetic testing for JAK2 mutation and EPO determination providing valuable clues for the diagnosis.
Disclosure: No disclosures..

EPR-323

Posterior reversible encephalopathy syndrome: twenty years of experience in a tertiary hospital

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Background and aims: The posterior reversible encephalopathy syndrome (PRES) is an entity whose physiopathology, triggers and radiological characteristics are not clearly established.
Methods: Retrospective analysis of patients diagnosed with PRES between 2000 and 2020.
Results: 27 patients were included (51.9% women), with mean age of 54.0±16.3 years. Seven patients had arterial hypertension. 17 patients were receiving PRES-associated drugs (10 of them calcineurin inhibitors). Two patients developed PRES in the context of eclampsia. 14 patients had high blood pressure at onset. The most frequent clinical manifestations were low level of consciousness; followed by seizures, visual alterations, headache, aphasia and hemiparesis. Six patients had acute renal failure. CSF analysis was normal in all patients when available. Cranial MRI was performed in 23 patients: posterior pattern was observed in 13 patients, anterior pattern in one patient, holohemispheric pattern in six patients, diencephalic and brainstem pattern in six patients. Two patients had only cortical involvement. 11 patients had altered diffusion sequence of which seven showed restriction in ADC map. 1 patient has subarachnoid haemorrhage, two patients intraparenchymatous haemorrhage and one patient deep microbleeds. Vascular imagining was normal in all patients. Eight patients required ICU admission and three patients died. At discharge more than 80% of patients were independent. Control brain MRI showed resolution or improvement in all cases when available.
Conclusion: In our series the most frequent trigger were drugs, mainly calcineurin inhibitors. The typical posterior radiological pattern was not observed in a high percentage of patients so its absence should not rule out the diagnosis of PRES.
Disclosure: N/A

EPR-324

Development of a Conceptual Model of Wilson Disease for Patients with a History of Neurological Symptoms

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Background and aims: Wilson disease (WD) is a disorder of impaired biliary excretion of copper that leads to its accumulation in the liver and extrahepatic tissues, including the brain and spinal fluid. Often diagnosed in adolescence or early adulthood, WD gradually poses significant burden to patients and caregivers. The aim of this study was to assess how the disease and its treatment impact the lives of WD patients who have a history of neurological symptoms.
Methods: A preliminary conceptual model (CM) of the WD patient experience was developed based on results of a targeted literature review and clinician interviews. This information was used to guide semi-structured, one-on-one qualitative telephone interviews with WD patients with a documented history of neurological symptoms. Patient interviews provided further insight into the signs, symptoms and impacts (i.e., 'concepts') of WD including degree of bother, change over time, and identification of 'salient concepts' (concepts experienced by 10 patients with an average peak bother rating of 5 on 0 [not at all] – 10 [very bothersome] bother scale). These interviews informed the final CM.
Results: 20 patients (Europe, n=11; US, n=9; ages, 15–68 years) reported a wide range of current and past hepatic (n=26), neurologic (n=20), and psychiatric (n=13) symptoms. Four hepatic, five neurologic, and six psychiatric symptoms emerged as salient (Figure). These symptoms impact many aspects of life including physical, emotional, and social wellbeing.

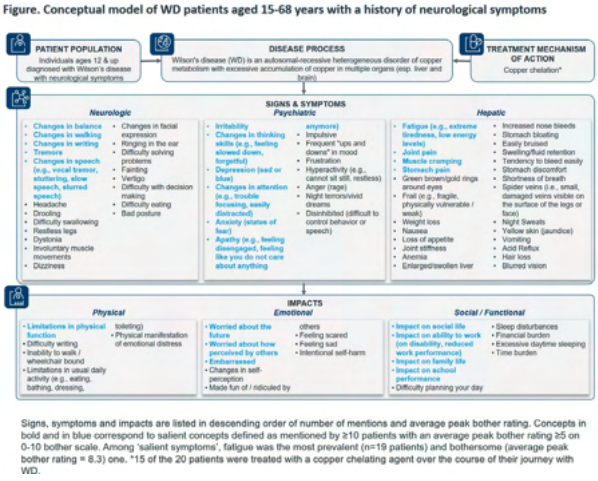

Figure. Conceptual model of WD patients aged 15-68 years with history of neurological symptoms

Conclusion: The final CM depicts a wider range of bothersome neurological, hepatic, and psychiatric symptoms that disrupt patients' lives more than was previously recognized.
Disclosure: The study was funded by Alexion Pharmaceuticals, Inc. Megan Teynor is an employee of Alexion Pharmaceuticals, Inc. and may own stock/stock options in that company.

EPR-325

COVID-19 & Safety Update: OPTIMISE: MS – a prospective, real word pharmacovigilance study in MS

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Background and aims: Therapeutic options in MS have increased rapidly, but real-world safety data is limited. Safety signals have emerged from clinical trials and early clinical experience with newer MS therapies, however the rates at which these occur in a real-world, UK MS population is unknown.

Methods: OPTIMISE:MS is a longitudinal observational study that will recruit at least 4,000 people with MS eligible for DMT from centres across the UK. It will follow them up for at least five years in the first instance using electronic case records. Serious adverse events (SAEs), DMT use and disease outcomes will be captured.

Results: Since its initiation in June 2019, 1,700 people with MS have enrolled, with mean age 44.6 (SD 11.0); mean disease duration 8.7 years (SD 7.3)); 71% female. 95% of the study population have RRMS and 56% were receiving DMT immediately prior to consent. Since the occurrence of COVID-19 lockdowns in the UK, data on the occurrence of COVID-19 infections in the population has also been captured. We have observed 11 COVID-19 cases on the OPTIMISE electronic case record data capture system. No cases of severe COVID requiring hospitalisation have been recorded.

Conclusion: This study has the potential to deliver clinically meaningful data on the association of MS DMT with serious adverse events in a real-world population. The association of SAEs with lymphopaenia, and prior DMT/DMT switching will be studied. Rates of malignancies and opportunistic infections will be of particular interest owing to the immunosuppressive nature of many DMTs.

Disclosure: N/A

Spinal cord and root disorders; Peripheral nerve disorders

EPR-326

Vestibular impairment in Charcot-Marie-Tooth type 1A and Hereditary Neuropathy with Liability to Pressure Palsies

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Background and aims: To examine the vestibulo-ocular reflex VOR characteristics in Charcot-Marie-Tooth type 1A (CMT1A) and hereditary neuropathy with liability to pressure palsies (HNPP) using the video head-impulse test (vHIT).
Methods: 22 patients with CMT1A and 17 patients with HNPP were recruited. Three-dimensional vHIT was performed. VOR gain, refixation saccade prevalence and first saccade amplitude, onset latency, peak velocity and duration were examined and compared against age-matched normal controls (NC).
Results: In CMT1A and HNPP gait imbalance was reported in 81.8% and 58.8% of patients, resulting in recurrent falls in 63.6% and 23.5% of patients. 41% of CMT1A and 11.7% HNPP patients had reduced VOR gain. Refixation saccade prevalence for horizontal, anterior, and posterior canals (HC, AC, PC) were 5,928, 2,119, 5,438 in CMT1A, 5,933, 3,328, 6,747 in HNPP, and 5,428, 1,316, 5,436 in NC. 1st saccade onset latency was longer in HC and PC in CMT1A compared to NC ($p<0.05$). In CMT1A VOR impairment was associated with higher CMTES score, longer duration of disease and higher total ONLS score ($p<0.05$), and VOR gain was lower for PC in patients with history of recurrent falls ($p<0.05$).
Conclusion: VOR impairment and prolonged onset latency of the refixation saccades were found in CMT1A cohort. These findings may relate to demyelinating process involving the VOR pathways. Recurrent falls and underlying vestibular impairment supports incorporation of vestibular exercises to standard physiotherapy in patients with CMT1A.
Disclosure: Nothing to disclose.

EPR-327

NEuropathies Related to Virus E in Switzerland (NERVES)

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[1] Lugano, Switzerland, [2] Sion, Switzerland, [3] Geneva, Switzerland, [4] Berne, Switzerland, [5] St. Gallen, Switzerland, [6] Luzern, Switzerland, [7] Zurich, Switzerland, [8] Fribourg, Switzerland, [9] Basel, Switzerland, [10] Lausanne, Switzerland, [11] Bellinzona, Switzerland

Background and aims: Previous studies have shown that hepatitis E virus (HEV) can trigger 5–10% of Guillain Barré syndrome (GBS), 10% of neuralgic amyotrophy (NA) and facial palsy. We aim to estimate the prevalence of HEV infection in these neuropathies.
Methods: Prospective, multicentre, case-control study. Since August 2019, we test for HEV (IgM and IgG serology; serum HEV RNA in case of positive IgM result) all newly diagnosed cases (= within one month from symptom onset) of GBS, NA and facial palsy referred to one of the 10 participating centres. Controls are healthy blood donors, matched for sex, age and geographical area.
Results: Acute HEV infection was detected in 4/25 (16%) cases of NA, in 1/40 (2.5%) case of GBS, and in 0/54 cases of facial palsy. The bilateral form of NA (5/25, 20%) occurred only in males and was associated with viral infections (HEV, n=2; Parvovirus B19, n=1; Epstein-Barr virus, n=1). one male with NA and acute HEV had symptoms outside the brachial plexus. All NA cases suffered from severe neuropathic pain at onset and about 50% had scapular dyskinesia. The most affected muscles in NA were infraspinatus, supraspinatus and deltoid. 17 NA cases were treated with oral steroids and one with a single course of intravenous immunoglobulin (2g/kg).
Conclusion: HEV infection can precede about 16% of NA cases, suggesting a parainfectious pathogenesis. HEV-related NA often has a bilateral involvement, with possible extra-brachial plexus damage. Only rarely (2%) GBS is preceded by HEV infection, and none of the facial palsy cases.
Disclosure: Nothing to disclose.

EPR-328

Spinal dural arteriovenous fistula (SDAVF) presenting with fatigable peripheral leg muscle weakness: a case-report

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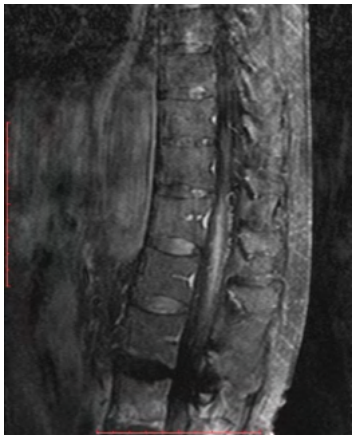
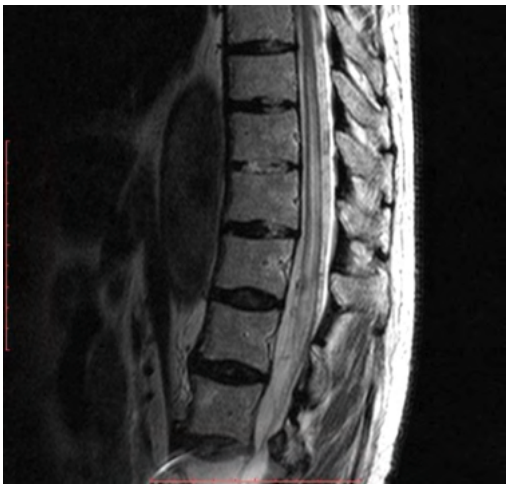
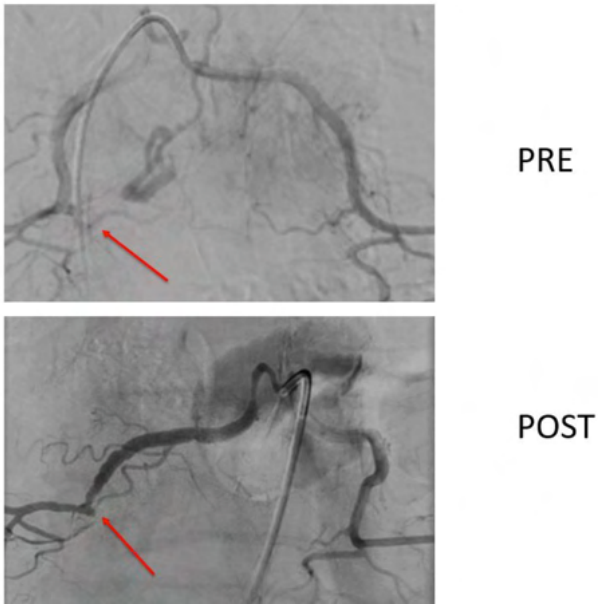
Background and aims: SDAVF is the most common spinal vascular malformation. However, misdiagnosis often occurs due to diverse symptoms with upper and lower motor neuron involvement, sensory disturbance and autonomic dysfunction.
Methods: Case-report
Results: A 72-year-old man was admitted to the neurology department due to slowly progressive gait impairment, characterized by frequent stumbling and fatigable peripheral leg muscle weakness over the last two years. He denied any pain, sensory abnormalities, bladder/bowel dysfunction, arm weakness, cramps or fasciculations. His past medical and family history were unremarkable. Neurological examination revealed impaired walking on toes exacerbating upon sustained activity, normal deep tendon reflexes, symmetric anterior tibialis weakness (4+/5 RC) and toe dorsiflexion (4/5 MRC) with no atrophy or sensory impairment. Biochemical analysis, lumbar spinal MRI, nerve conduction studies, electromyography and repetitive nerve stimulation (trapezius, abductor digiti minimi) were normal, whereas single-fiber electromyography(SF-EMG) of anterior tibialis was abnormal. Anti-AChR Abs were negative and there was no clinical response to pyridostigmine. Neurogenic cause of SF-EMG abnormality was suspected, and repetition of spinal neuroimaging was suggested. Spinal MRI revealed diffuse hyperintensity on T2-weighted images from T9 to conus medicullaris with gadolinium enhancing engorged perimedullary veins on T1-weighted images, indicative of SDAVF. Spinal catheter angiography confirmed the SDAVF(L4 level) and endovas-cular embolization with N-butyl-2-cyanoacrylate(NBCA) was successful. One month later, the patient was significantly improved.



Thoracic spine T1-weighted Magnetic Resonance Imaging (MRI) with gadolinium (Gd) demonstrating Gd+ enhancing tortuous engorged perimedullary veins around conus medicullaris, indicative of spinal dural arteriovenous fistula (SDAVF).



Thoracic spine T2-weighted Magnetic Resonance Imaging (MRI) depicting diffuse hyperintensity from T9 level to conus medicullaris, due to spinal cord edema.



Spinal catheter angiography demonstrating the SDAVF. Successful endovascular embolization with N-butyl-2-cyanoacrylate (NBCA).

Conclusion: We present an unusual case with progressive painless fatigable peripheral leg muscle weakness, initially mimicking a neuromuscular disorder but finally attributed to SDAVF. Careful neurological and neuroradiological evaluation is required for prompt diagnosis to prevent irreversible damage.
Disclosure: Nothing to disclose..

EPR-329

Neuromodulation of failed back surgery syndrome

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Background and aims: Failed back surgery syndrome (FBSS) is a disease with complex etiology. The incidence of 10–40% of patients after spinal surgery. The major randomized studies conclusive results about the superiority of spinal cord stimulation (SCS) with comparing medical treatment or repeat operative (evidence level 1B+). In case of inadequate efficiency recommended peripheral nerve stimulation/peripheral nerve field stimulation (PNS/PNFS) or sacral nerve root stimulation (SNRS) as a free-standing or add-on treatment.
Methods: The study comprised 108 patients with FBSS (females 65 (60%), disease duration was 8,7). A psychological evaluation was conducted of The Hospital Anxiety and Depression Scale (HADS). The impact of pain on quality of life was conducted on the Pain Quality of Life Scale (PQLS). All of patients have had successful the trial period, after that was implanted system for chronic neurostimulation: SCS – 94 (87%), PNS – 2 (1,8%), PNFS – 4 (3,7%) and hybrid stimulation: SCS+PNFS – 3 (2,8%), SCS+PNS – 1 (0,9%), SCS+SNRS – 2 (1,8%), SCS+intrathecal morphine pump (IMP) – 1(0,9%) and SCS+IMP+PNFS – 1(0,9%). All the patients have a complects medical treatment before neuromodulation.
Results: Mean follow-up of 53,8 months. The severity of pain has decreased (preVAS 8,7; postVAS 4), also decreased the severity attacks of pain (preVAS 10, postVAS 5,6). All of the patients reduced the dose of analgesic drugs. Decreased indicators of anxiety and depression (HADS-A and D scale -21%). PQLS indicators were improving for all patients.
Conclusion: Neurostimulation the patients with FBSS has high efficacy and a high level of evidence.
Disclosure: Nothing to disclose.

EPR-330

Acute myelopathies: Clinical, paraclinical and etiological study

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Background and aims: The causes of acute myelopathies are multiple requiring a rigorous diagnostic investigation and a prolonged follow-up.
Methods: Descriptive, retrospective study of 117 cases of acute myelopathies in the neurology department of the Military Hospital of Tunis over a 19-year period from January 1998 to December 2016. Patients meeting the criteria of the Transverse Myelitis Consortium Working Group. Clinical and paraclinical features have been studied.
Results: The sex ratio was 0.72. The average age of our population was 33±11 years old. Fever and/or influenza-like illness were reported by 6% of patients and initial spinal pain by 24% of them. The clinical examination showed a motor impairment in 83% of our patients, sensitive in 59% of cases and vesico-sphincterian in 33% of them. Medullary magnetic resonance imaging was abnormal in 82.1% of patients. The cervical cord is the most common location with 49.5% of cases. Cerebrospinal fluid analysis was abnormal in 52% of cases. All patients had intravenous coticotherapy. The functional course was favorable in 36% and stationary in 53% of the patients. The different etiologies found were distributed as follows: 46% multiple sclerosis, 14% systemic diseases, 12% idiopathic acute myelitis, 11% decompression sickness, 8% Devic optical neuromyelitis, 6% infectious myelitis or post-infectious and 3% ischemic myelitis.
Conclusion: Acute myelopathies come from a wide variety of etiologies. Determining a precise clinical and paraclinical profile can guide the diagnostic strategy and establish a prognosis for a more targeted support and a better evolution.
Disclosure: There is no conflict of interest.

EPR-331

HHV6 and immune-mediated meningoencefalomyelitis after check point inhibitors treatment for melanoma

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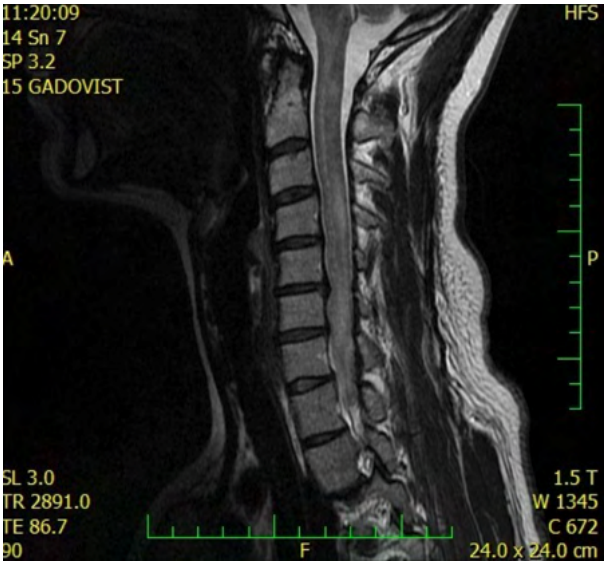
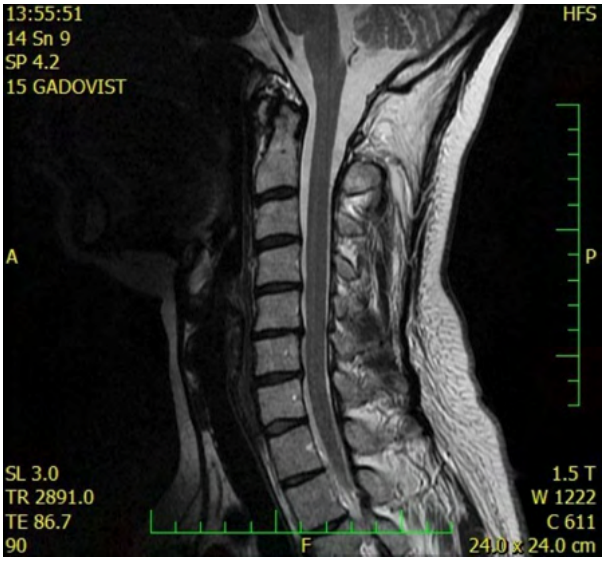
Background and aims: Immune checkpoint inhibitors (ICI) anti CTLA-4, PD-1 and PD-L1 inhibitors produce durable antitumor responses and have dramatically changed outcomes for patients with melanoma and other malignancies. However, this treatment provoke different immune-mediated toxicities, including immune-related neurological complications of the central or peripheral nervous system, the neuromuscular junction or muscle.

Methods: 42-years-old female treated for disseminated melanoma by nivolumab and ipilimumab presented fatigue, blurred vision, febrile, slight neck pain with projection into the fingers and pain on the chest. Objectively she developed only exaggerated reflexes on the upper and lower limbs.

Results: Initial cerebrospinal fluid (CSF) revealed protein-cytologic association with 168 elements/ul and CSF protein of 1.45 g/L. Magnetic resonance imaging (MRI) of the brain showed leukoencephalopathy with increased T2-FLAIR signal intensity in the periventricular, deep and subcortical white matter. MRI of the spinal cord showed longitudinally extensive myelitis (Fig.1). At the beginning we diagnosed HHV6-associated meningoencefalomyelitis with good clinical response to intravenous ganciclovir but later on when clinical and MRI progression was observed immune-mediated meningoencefalomyelitis was re-diagnosed. She was treated by 3g of methylprednisolone followed by oral prednisone of 20mg daily with significant clinical and MRI improvement of the brain and spinal cord (Fig.2).



MRI of cervical spine performed after the onset of symptoms showing myelitis



MRI of cervical spine two months after the onset with normal findings in the spinal cord

Conclusion: Although the immune-mediated neurological complications after ICI treatment are not very common, their incidence will increase. Investigating these patients requires urgent treatment (corticosteroids, antibiotics, antivirals, etc.) to prevent life-threatening complications together with exclusion of other differential diagnoses.

Supported by the Research project of Charles University, Progress Q35.

Disclosure: Nothing to disclose.

EPR-332

Abstract withdrawn

EPR-333

Queckenstedt's test in spinal cord compression revisited

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Background and aims: Jugular vein compression results in elevated cerebrospinal fluid pressure (CSFP), which can be measured during lumbar puncture. This maneuver was then termed Queckenstedt's test (Q-test) referring to the first description. This phenomenon is related to an increase in intracranial CSFP and its transmission to the lumbar compartment under physiological conditions. We aim to revisit Q-test literature and determine its potential relevance for today.

Methods: We searched PUBMED and PMC entries from 1916-2020 in English, French, German, and Italian language with key word "Queckenstedt". Additionally, personal and college libraries and non-electronical resources were searched for texts on Q-test.

Results: About 100 years ago Q-test was used for diagnosing spinal block – i.e., complete narrowing of the spinal canal – with the test specificity considered high while sensitivity was rated moderate to low. Contraindications other than those considered in any lumbar puncture are not postulated. Nowadays, spinal block is reliably detected in MRI, however, Q-test and advanced CSFP analyses are promising complimentary investigations in ambiguous conditions of cord compression.

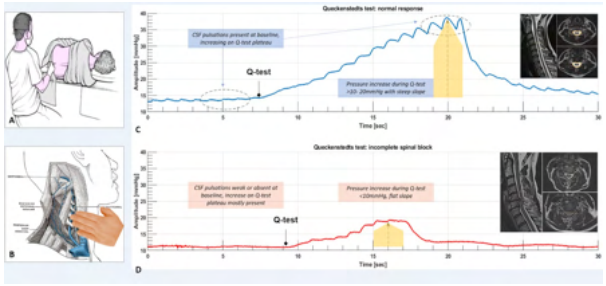

Figure 1

Conclusion: To our best knowledge this is the first comprehensive review of historical Q-test- studies in English/French/German/Italian language. Q-test is nowadays not routinely used to diagnose spinal compression, but may be selectively used to detect CSFP disturbances, which is less conclusive with MRI and CT.

Disclosure: This work was supported by the Swiss Paraplegic Foundation, Nottwil, Switzerland and the Balgrist Foundation, Zurich, Switzerland. No competing interests result from the funding.

ePresentations

Monday, June 21 2021
Neuro-ophthalmology/neuro-otology

EPR-334

Risk for generalization in ocular onset myasthenia gravis: experience from a neuro-ophthalmology clinic

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Background and aims: Conversion to generalized myasthenia gravis (GMG) within the first two years has been reported in 18% to 85% of patients with ocular myasthenia gravis (OMG). The aim of the study was to investigate the risk factors for generalization in patients with OMG admitted to a neuro-ophthalmology clinic and to determine if there were differences between patients with GMG with predominant bulbar (GMG-B) or extremity muscle (GMG-E) involvement according to the 6th and 24th-month Myasthenia Gravis Foundation of America classification ranks.
Methods: Patients with OMG who were followed-up for at least 24 months were retrospectively analyzed. Demographic, clinical, laboratory features and treatment strategies that can be associated with generalization and time to generalization were evaluated.
Results: Of the 139 patients with OMG, 54 (39%) showed generalization with a mean time of 10.3 (range, 2-24) months. GMG-B and GMG-E were diagnosed in 31 (22.3%) and 23 patients (16.5%), respectively. Seropositivity for acetylcholine receptor and muscle-specific tyrosine kinase antibodies, abnormal single-fiber electromyography (SFEMG), and the presence of thymic abnormalities (thymoma and hyperplasia) were factors associated with generalization on multivariate analysis without a significant difference between the GMG-B and GMG-E groups. In addition, an abnormal repetitive nerve stimulation test was related to a shortened time to generalization. Bilateral ptosis at onset was found as a risk factor for generalization.
Conclusion: : In a neuro-ophthalmology clinic, bilateral ptosis as an initial feature of OMG must be approached cautiously because it may be the first sign of impending GMG.
Disclosure: Nothing to disclose.

EPR-335

Infantile nystagmus syndrome in adulthood: a series on its misdiagnosis

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Background and aims: Infantile nystagmus syndrome (INS) is a common benign cause of abnormal ocular movement during childhood. However, INS might reach adulthood unnoticed and mimic acquired forms of jerk nystagmus. We aimed to highlight the pitfalls of INS diagnosis in adulthood.
Methods: Retrospective analysis of patients data, referred to our clinic with the final diagnosis of INS, from January 2016 to August 2020.
Results: We included 12 INS patients (10 jerk-, two pendular-type). There were 58.3% females (n=7), with a median age of 58 (interquartile range [IQR]=35) years. Symptoms leading to the referral, apart from the nystagmus itself, were imbalance with/without vertigo (n=6), oscillopsia/blurred vision (n=4) and diplopia plus oscillopsia (n=2). Working diagnosis upon referral were central nervous system lesion (n=5), peripheral vestibular disorder (n=2), and hereditary ataxia (n=1). Before referral, patients had had a median number of 4 (IQR=5) clinical encounters and had performed a median of 2 (IQR=3) exams due to the nystagmus. In the clinic, all patients showed bedside clues leading to INS diagnosis, including nystagmus attenuation in darkness (n=9) or with convergence (n=2) and presence of a null-point (n=5). Video-oculography (VOG) further showed exponential increasing/decreasing nystagmus slow-phase (n=8), presence of a foveation period (n=7), inverted optokinetic responses (n=4), and specific nystagmus waveforms (ie. pendular, pseudo-cycloid, pseudo-jerk; n=4). Median time from nystagmus detection to INS diagnosis was 13.5 (range, 0–174) months.
Conclusion: Undiagnosed INS in adulthood seems to pose a diagnostic challenge. Bedside clues here provided and the use of VOG might help in its easier diagnosis.
Disclosure: Nothing to disclose.

EPR-336

Color Vision and Contrast Sensitivity as Biomarkers of Preclinical Neurodegeneration in Huntington's disease

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[1] Department of Neurology, Nizhny Novgorod, Russian Federation, [2] Volga District Medical Center of Federal Medical and Biological Agency of Russia, Nizhny Novgorod, Russian Federation, [3] Yoshkar-ola, Russian Federation

Background and aims: The aim of the study was to investigate color vision and contrast sensitivity (CS) in Huntington's disease (HD).
Methods: There were involved 21 pre-manifest gene carriers, 23 manifest HD patients and 31 healthy controls. The groups were age-, sex-, intraocular pressure-, and mean refractive error-matched. CAG (cytosine-adenine-guanine) repeat expansion size in the huntingtin gene, disease duration, and a motor function score according to the UHDRS were evaluated in HD patients. All patients underwent a thorough neurological and ophthalmic examination including CS evaluation using Freiburg Vision Test (FrACT) and color vision assessment with the use of original computer program (http://doi.org/10.17691/stm2019.11.2.11).
Results: CS in manifest HD patients was reduced compared with controls. The CS log inversely correlated with CAG repeat expansion size. Color differentiation thresholds in both manifest HD patients and pre-manifest gene carriers were higher than in the control group in red, green and blue colors. Color differentiation thresholds in green and blue correlated with the UHDRS score. When plotting ROC curves, the differentiation threshold for green and blue color had been established to have high diagnostic value for distinguishing between the control and pre-manifest gene carriers.
Conclusion: The study results indicate visual sensory deprivation in HD. Color vision disturbances develop early at the pre-manifest HD stage, ahead of the CS decrease signifying early damage to the parvocellular vision pathway. Color differentiation thresholds proved to be a promising biomarker for early diagnosis of neurodegenerative processes.
Disclosure: Nothing to disclose.

EPR-337

Vestibular rehabilitation with low-frequency rotatory chair in vestibular migraine and migraine-related vestibulopathy

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Background and aims: Vestibular migraine (VM) and migraine-related vestibulopathy (MRV) are common dizziness causes. Vestibular rehabilitation (VR) has been suggested as a successful intervention in MRV. The effectiveness of VR as a therapeutic option for VM still lacks confirmation. Particularly, the effect of VR with rotatory chair protocol (RCP) in VM has rarely been assessed.
Methods: Retrospective analysis of prospectively collected data referring to patients with VM diagnosis in an Otoneurology unit of a tertiary centre who underwent VR which added low-frequency RCP including visual fixation to postural, balance and gait training exercises, pharmacological measures, sleep hygiene, and dietary and behavioural modifications in the acute phase, compared with patients with the diagnosis of MRV. VR effectiveness was assessed with dizziness handicap inventory (DHI).
Results: We found 38 patients, 58% (n=22) with VM. Global mean age was 48.13±15.85 years with no significant age nor gender differences between VM and MRV groups ($t(36)=1.295$, $p=0.20$; $p=0.15$, respectively). In VM, median total DHI score after VR (10.5±24) was significantly lower than median total DHI score before VR (80±24), $Z=-4.107$, $p<0.01$, $r=-0.62$. In MRV, median total DHI score after VR (24±22) was also significantly lower than median total DHI score before VR (72±22), $Z=-3.517$, $p<0.01$, $r=-0.62$. DHI score variation was not significantly different between the two groups ($t(36)=-0.765$, $p=0.22$).
Conclusion: VR including low-frequency RCP with visual fixation seems an effective option in patients with VM and MRV. Further studies with larger samples, complementary clinical and neurophysiological evaluation and control of simultaneous therapeutic interventions are needed to validate this rehabilitation strategy.
Disclosure: Nothing to disclose.

EPR-338

Unreliable pupillary light reflex in hereditary transthyretin amyloidosis patients

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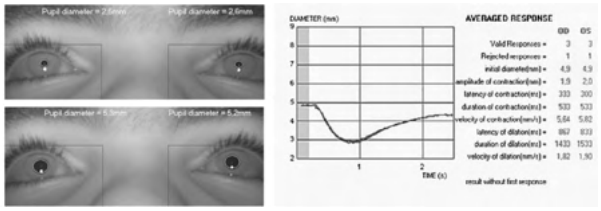
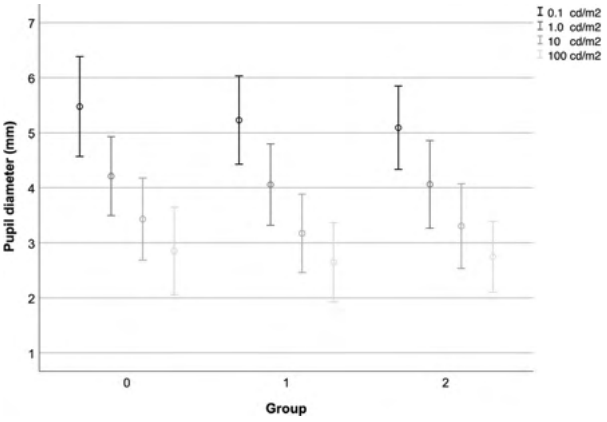
Background and aims: Hereditary transthyretin amyloidosis (hATTR) manifests as a progressive neurodegenerative disease, characterized by the accumulation of TTR in the peripheral nerves, brain and eyes. The presence of scalloped irises is considered a biomarker of intraocular TTR deposition and it is associated with glaucoma and retinal angiopathy, Our purpose is to analyze the pupillary light reflex in hATTR patients with scalloped pupils.

Methods: Prospective cross-sectional observational study in patients with hATTR with unilateral scalloped iris. Pupillary light reflex of scalloped iris eyes (21 eyes) were compared with non-scalloped iris eyes (21 paired eyes of the same patients) and also with a control group of 20 healthy eyes, using automatic computerized pupillometry (Metrovision® MonPack One).



Pupillometry examination case example.

Results: No patient presented evident involvement of the cranial nerves. No significant differences were found in the pupillary diameters under standardized lighting conditions (static pupillometry) among groups. In dynamic pupillometry, the amplitude of contraction, the velocity of contraction and the velocity of dilation were statistically significantly lower in eyes with scalloped iris, comparing both with the contralateral non-scalloped iris eyes ($p<0.001$ for all) and with eyes from healthy subjects ($p<0.05$ for all).



Graph representing static pupillometry diameters by illumination conditions by group. Marks represent mean and bars represent standard deviation. Illumination units are candle/meter^2 (cd/m^2).

Conclusion: The pupillary light reflex may not be reliable to evaluate neurological status in hATTR patients. In the presence of an altered pupillary light reflex a prompt ophthalmological examination should be considered to look for scalloped iris and glaucoma.

Disclosure: No financial disclosure.

EPR-339

Examination of vestibular function to differentiate between vestibular disorders: a study in 2,101 patients

V. Mavrodiev [1], M. Strupp [2]
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Background and aims: In Menière's disease (MD), a dissociation between a "pseudo-normal" video head-impulse test (vHIT), measuring the function of the vestibulo-ocular reflex (VOR) in the high-frequency range, and normal caloric testing, measuring VOR function in the low-frequency range, has been reported. This finding can be helpful in particular for the differentiation between MD and vestibular migraine (VM). The aim of this study was to determine the sensitivity, specificity, and positive and negative predictive values (PPV and NPV) of this dissociation for the differentiation not only between MD and VM but also between MD and other vestibular diseases
Methods: We performed a retrospective multicentric analysis of 2,101 patients. The examination group consisted of 1,100 patients: 57% with MD according to the diagnostic criteria of the Bárány Society and 43% with VM. The comparison group consisted of 1,001 patients with other peripheral, central or functional vestibular disorders.

Group	N	Composition
Examination group	1100	627 – Menière Disease 473 – vestibular Migraine
Comparison group	1001	Other central and peripheral vestibular disorders – functional vertigo, Neuronitis vestibularis etc

Table 1. Patient research collective

Results: For the dissociation between a pseudo-normal vHIT and pathological caloric testing, statistical analysis revealed the following results: MD vs VM: specificity 83.6%, sensitivity 58.9%, PPV 82.6%, NPV 60.5%. MD vs all examined vestibular disorders (including VM): specificity 83.5%, sensitivity 58.9%, PPV 60.3%, NPV 82.7%.

Meniére Disease vs. Vestibular Migraine		
369 true positive	78 false positive	PPV 82,6 %
258 false negative	395 true negative	NPV 60,5 %
Sensitivity 58,9 %	Specificity 83,6 %	

Meniére Disease vs. other vestibular disorders (without vestibular migraine)		
369 true positive	165 false positive	PPV 69,1 %
258 false negative	835 true negative	NPV 76,4 %
Sensitivity 58,9 %	Specificity 83,5 %	

Meniére Disease vs. All (vestibular migraine plus others)		
369 true positive	243 false positive	PPV 60,3 %
258 false negative	1230 true negative	NPV 82,7 %
Sensitivity 58,9 %	Specificity 83,5 %	

Table 2. Diagnostic power of the dissociation between a "pseudo-normal" vHIT and a pathological caloric testing

Conclusion: This dissociation has a high specificity and PPV for differentiation between MD and VM. For the differentiation between MD and all other examined vestibular disorders, when negative it rules out MD with a high predictive value.
Disclosure: VM does not have any COI. MS is Joint Chief Editor of the Journal of Neurology, Editor in Chief of Frontiers of Neuro-otology and Section Editor of F1000. MS received further honoraria - character limiation reached

EPR-340

Etiology of bilateral vestibulopathy: a retrospective analysis in 394 patients

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Background and aims: Bilateral vestibulopathy (BV) is a chronic vestibular disorder and the most common known cause of postural instability in the elderly. Symptoms typically worsen in darkness or on an uneven surface. Studies show that BV remains idiopathic in 60–75% of cases despite extensive diagnostics.
Methods: We performed a retrospective analysis with data from 394 patients with BVP and probable BVP according to the current diagnostic criteria of the Bárány society focusing on pre-existing medical conditions, medication use, as well as known and possible diseases which can lead to BVP. We also estimated the certainty of the causality of the etiology.
Results: Statistical analysis revealed the following results on the etiology of BVP causes: 49% idiopathic; 12% antibiotics, 11% of which were gentamicin; 11% degenerative disorders with CANVAS as the most common disorder; 9% bilateral Menière's disease (MD); 6% autoimmune; 6% postinfectious, including meningitis; 2% chemo- or radiotherapy; 5% other causes. Out of the 51% patients with a known BV etiology, the causality was clinically certain in 65.5% of the cases and probable in 34.5%. Additional sensory polyneuropathy was diagnosed in 29% of patients.
Conclusion: In half of the cases, the underlying etiology of BVP remains unclear. The most frequent cause is ototoxic antibiotics. Bilateral MD seems to be underestimated as a cause partly due to possible difficulties differentiating MD from other vestibular syndromes. Additional sensory polyneuropathy was found frequently which worsens the symptoms. In future research the focus should be on possible underlying causes of what is currently classified as "idiopathic BVP".
Disclosure: VM does not have any COI. MS is Joint Chief Editor of the Journal of Neurology, Editor in Chief of Frontiers of Neuro-otology and Section Editor of F1000. MS received further honoraria – character limiation reached

EPR-341

Diagnostic Agreement of Video Oculography and MRI for Internuclear Ophthalmoplegia in Multiple Sclerosis Patients

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Background and aims: Internuclear ophthalmoplegia (INO) affects 20–30% of patients with multiple sclerosis (MS). There is no established gold-standard for diagnosing INO. Not all patients with INO show a typical lesion on MRI. Early INO detection is important for subtyping, treatment and prognosis of MS. In one study1, 71% of clinicians missed the diagnosis of subtle INO, that was otherwise detected using video oculography(VOG).
Methods: We prospectively compared MRI and VOG in 70 MS patients and 28 healthy volunteers to compare their diagnostic agreement. The saccadic versional-disconjugacy-index (VDI, peak velocity ratio of abducting to adducting eye) was calculated f and a cutoff (upper 95th-percentile of normal) was defined for INO diagnosis2. For each patient a concurrent MRI was reviewed by three experienced neuro-radiologists independently. The consensus MRI score was compared to the VDI for each patient.
Results: In 44 patients, the two tests agreed. In 19 cases, the tests demonstrated contradicting results: 11 patients were INO-positive on VOG with no identifiable lesion on MRI, whereas eight patients demonstrated a lesion on MRI, with no detectable INO on VOG. Compared to VOG, MRI had a positive percent agreement (PPA) of 46% and a negative percent agreement (NPA) of 92%. Conversely, VOG had 60% PPA and 87% NPA compared to MRI.
Conclusion: VOG was more sensitive for detecting INO than MRI. Consequently, a normal VOG is suitable to rule out INO, while a positive MRI is suitable to rule in INO with certainty. VOG is a simple, quick and non-invasive test to help diagnose INO.
Disclosure: Nothing to disclose.

EPR-342

Primary or secondary chronic functional dizziness: Does it make a difference? - a DizzyReg study in 356 patients

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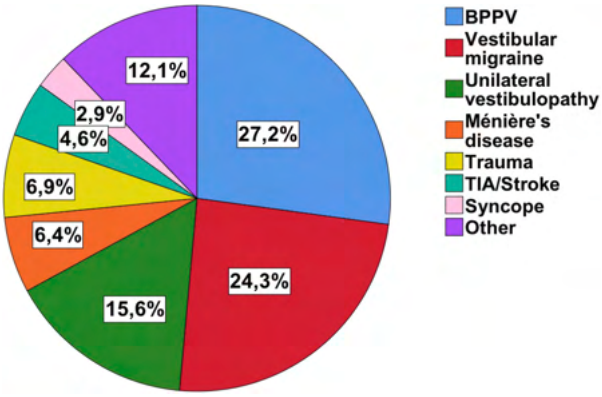
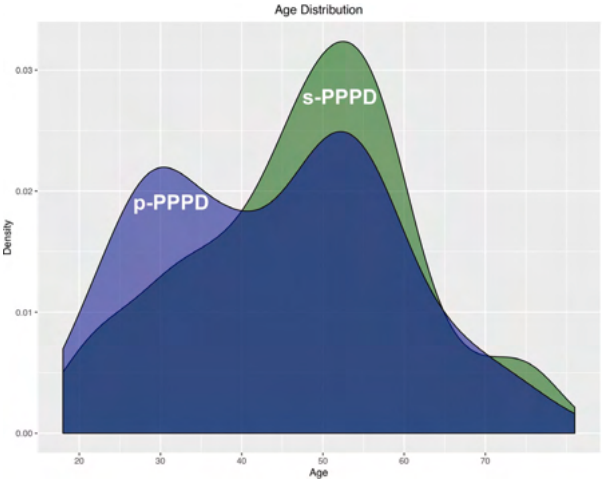
Background and aims: "Persistent postural-perceptual dizziness" (PPPD) can originate secondarily after an organic disorder (s-PPPD) or primarily on its own (p-PPPD). The aim of this database-driven study in 356 patients from a tertiary vertigo center was to describe demographic and clinical features in p-PPPD and s-PPPD patients.

Methods: Patients received detailed vestibular testing with neurological and neuroorthoptic examinations (video-oculography during water caloric stimulation, video head-impulse test, subjective visual vertical, static posturography). All patients answered standardized questionnaires (Dizziness Handicap Inventory, DHI; Vestibular Activities and Participation, VAP; Euro-Qol-5D-3L).

Results: 195 patients (55%) were categorized as p-PPPD and 162 (45%) as s-PPPD, with female gender slightly predominating (=56%:44%), particularly in the s-PPPD subgroup (64%). The most common somatic triggers for s-PPPD were benign paroxysmal positional vertigo (27%), and vestibular migraine (24%). Overall, p-PPPD patients were younger than s-PPPD patients (44 vs. 48 years) and showed a bimodal age distribution with an additional early peak in young adults beside a common peak at the age of 50–55. The most sensitive diagnostic tool was posturography, revealing a phobic sway pattern in 50% of cases. s-PPPD patients showed higher handicap and functional impairment in DHI (47 vs. 42) and VAP (9.7 vs. 8.9). EQ-5D-3L was not differenent between both groups. In p-PPPD, anxiety (20% vs. 10%) and depressive disorders (25% vs. 9%) were more frequent.



Pie chart of somatic triggers for secondary PPPD (n=162) reported as relative percentages.



Age distribution density curve in primary and secondary PPPD. Primary (blue) and secondary PPPD (green) show a common peak at 50–55 years of age, whereas p-PPPD shows an additional peak in in young adults between around 30 years of age.

Conclusion: This retrospective study in a large cohort showed relevant differences between p- and s-PPPD patients in terms of demographic and clinical features, thereby underling the need for careful syndrome subdivision for further prospective studies.

Disclosure: Nothing to disclose.

Sleep disorders

EPR-343

Effect of short-term and long-term use of melatonin in young rats on behavioral parameters in adulthood

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Background and aims: Melatonin (MTL) acts not only on circadian rhythm, but also on neuronal modulation. In the hippocampus, MTL receptors are found in regions of the mossy fiber pathway (CA3) and Schaffer collateral pathway (CA1). MTL significantly alters synaptic transmission and long-term potentiation in CA1, it is an excitatory via that has synapses probably related to the formation of episodic memory, changes in it can generate behavioral modifications. With the knowledge of MTL receptors in the brain and the pathways that are linked to cognition, it corroborates the need for studies that evaluate the performance of animals and their actions after prolonged exposure to the drug during the youth until reaching adult life.
Methods: 43 male Wistar rats (250–350g) were used and divided into three groups: group Saline + saline (n=13); MLT + short-term melatonin group (n=15), and MLT+ long-term melatonin group (n=15).
Results: The use of MLT did not result in significant behavioral changes for depressive behavior. However, a decrease in locomotor activity was found in the group of short term MLT treatment and it was verified responses of increased social interaction, decreased anxiety-like behavior and improved memory and learning only the MLT long-term group.
Conclusion: Since there was no adverse effect on the cognition of the animals studied, MTL is an interesting alternative to be used during the neurodevelopment period.
Disclosure: The authors report no disclosure.

EPR-344

Complementary and alternative medicine use in narcolepsy

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Background and aims: Narcolepsy is a rare chronic brain disorder. Management includes non-pharmacological and symptomatic pharmacological treatment. Complementary and alternative medicine (CAM) use is frequent (30-45%) in the general population in Germany. The aim of our study was to evaluate the frequency and patient characteristics of CAM use in German narcolepsy patients.
Methods: For assessment an online survey was used. Demographic, disease-related data (i.e. symptoms, medication); and frequency and impact of CAM use were assessed. 23 commonly used CAM methods were predetermined on the questionnaire. They were divided in five subgroups: holistic medical systems, biological-, energetic, mind body-, and body based therapies.
Results: 172 completed questionnaires were included into analysis (n=44 male, n=127 female; n=121 narcolepsy type 1 (NT1), n=51 type 2 (NT2)). 32 % (n=55) of the patients reported CAM use regarding narcolepsy in the present or past. Most frequently, biological therapies, vitamins and trace elements (58%) in particular; and mind body therapies – i.e. meditation (45.5%) were used. Body based and mind body CAMs were used particularly by NT1 patients (22% vs. 10% NT2; and 34% vs. 24%). 26/55 patients using CAM described this as helpful (NT1: 61%; NT2: 40%). 16% of all 172 patients did not take any pharmacological treatment, but 43% of them used CAM.
Conclusion: The use of CAM in narcolepsy patients is common (1/3), however the impact seems to be limited. The common use of mind body therapies points to the need of further psychological well-being.
Disclosure: Nothing to disclose.

EPR-345

The Arousal Disorders Questionnaire: a new screening tool for Confusional Arousals, Sleepwalking and Sleep Terrors

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Background and aims: Arousal Disorders (DoA) include Confusional Arousals, Sleepwalking and Sleep Terrors. DoA diagnosis is mainly clinical but no validated questionnaires exist for DoA screening according to the criteria of the International Classification of Sleep Disorders, third Edition. Recently our group proposed the Arousal Disorders Questionnaire (ADQ) as a new diagnostic tool for DoA diagnosis. The objective of this study was to evaluate the diagnostic accuracy of the ADQ in a sleep and epilepsy center.
Methods: One interviewer blinded to clinical and video-polysomnographic (VPSG) data administered the ADQ to 150 patients consecutively admitted to our Sleep and Epilepsy Centers for a follow-up visit. The final diagnosis, according to VPSG recordings of at least one major episode, classified patients either with DoA (DoA group) or with other sleep-related motor behaviors confounding for DoA (nDoA group).
Results: 47 patients (31%) composed the DoA group; 56 patients with REM sleep behavior disorder, 39 with sleep-hypermotor epilepsy, six with night eating syndrome, and two with drug-induced DoA composed the nDoA group. The ADQ had a sensitivity of 72% (95% CI: 60–82) and a specificity of 96% (95% CI: 89–98) for DoA diagnosis; excluding the items regarding consciousness and episode recall, sensitivity was 83% (95% CI: 71–90) and specificity 93% (95% CI: 86–97).
Conclusion: The ADQ showed good accuracy in screening patients with DoA in a sleep and epilepsy center setting. Diagnostic criteria related to cognition and episode recall reduced ADQ sensitivity, therefore a better definition of these criteria is required, especially in adults.
Disclosure: Nothing to disclose.

EPR-346

Solriamfetol in the treatment of narcolepsy: real-world experience from the first 100 patients

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Background and aims: Narcolepsy is a rare chronic neurological disorder whose main symptoms are excessive daytime sleepiness (EDS) and cataplexy. In early 2020, solriamfetol, a norepinephrine and dopamine reuptake inhibitor was approved in the EU for the treatment of excessive daytime sleepiness in narcolepsy and obstructive sleep apnea. The aim of this prospective observational study was to assess efficacy, possible side effects, existing co-medication and co-morbidities in patients with narcolepsy in daily clinical practice.
Methods: Adult patients with narcolepsy type 1 and 2 were included in the study. Data on demographics, clinical characteristics, co-morbidities, and medication before and after initiation, add-on or switch of treatment (T0 and three months later) were collected. The Epworth Sleepiness Scale (ESS) was also used to assess daytime sleepiness.
Results: 100 consecutive patients were included. Interim results of 42 patients showed that 15 (36%) patients stopped taking the drug due to lack of efficacy (60%), or side effects (26.7%). In 27 patients, ESS score improved from 16.0 to 14.0. Surprisingly, cataplexy and nocturnal sleep also improved in 38% (33% respectively) of patients. Solriamfetol was most frequently used at the dose of 150 mg/day (45%). Side effects occurred in 33% of all 42 patients and included headache, cardiovascular and psychological complaints.
Conclusion: These first real-world results on solriamfetol showed a good effect on EDS. The drug was mostly well tolerated with headaches (29.5%) being the most frequent occurrence.
Disclosure: This was not an industry supported study. UK received fees for lecturing and consulting services from AOP Orphan Pharmaceuticals, Bioprojet Pharma, Harmony Biosciences, Jazz Pharma, Takeda Pharmaceutical, UCB Pharma.

EPR-347

Idiopathic hypersomnia: a homogeneous or heterogeneous disease?

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Background and aims: Idiopathic hypersomnia (IH) is a rare orphan disease characterized by excessive daytime sleepiness, frequently accompanied by prolonged nocturnal sleep and difficulties awakening, termed sleep inertia or sleep drunkenness (SI). Severe sleepiness usually causes a greater handicap in IH than in narcolepsy.
Methods: 43 IH patients (17 male, mean age 42.8±SD 12.2 years, range 20–67) diagnosed in the past 20 years were invited for a clinical examination to manifestations and severity of the disease, as well as clinical comorbidities. The patients completed a set of questionnaires scoring sleepiness, SI, fatigue, depression, anxiety, circadian preference, and quality of life.
Results: IH patients were divided according to the duration of nocturnal sleep at the time of their diagnosis into two cohorts: (1) with normal sleep duration (n=25, 58.1%) and (2) with long sleep duration (n=18, 41.9%). Women markedly prevailed in the 2nd cohort (n=14, 77.8%). Age at disease onset was younger in the group with long sleep duration (21.2±11.4 years versus 28.1±13.6 years, p=0.028), their MSLT latency was longer (7.2±3.7 minutes versus 5.1±1.7 minutes, p=0.005), a history of SI prevailed (p=0.005), and daily naps were mostly non-refreshing (p=0.014). Additionally, questionnaires in the group with long sleep duration showed more severe SI (p=0.007), fatigue (p=0.004), and a tendency towards evening chronotype (p=0.001).
Conclusion: IH patients with long sleep duration differ clinically and by objective measures at the time of diagnosis and in long-term follow up from IH patients without long 24-hours sleep time. In our opinion, they represent an independent clinical entity.
Disclosure: The study was supported by Ministry of Health of the Czech Republic, grant nr. NU20-04-00088

EPR-348

A double-blind randomized study with video analysis evaluating Nelotanserin as symptomatic treatment for RBD in DLB/PDD

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Background and aims: Rapid eye movement sleep behavior disorder (RBD) is frequent in dementia with Lewy bodies (DLB) and Parkinson's disease dementia (PDD), and poses a risk of injury to patients and their bed partners. We assessed the efficacy of nelotanserin, a selective 5-HT(2A) inverse agonist, for symptomatic treatment of RBD using systematic video analysis.
Methods: This was a phase 2 multicenter study in DLB or PDD with video polysomnography (vPSG)-confirmed RBD. After a single-blind placebo run-in period, patients meeting eligibility criteria entered a 4-week double-blind treatment period (1:1 ratio with nelotanserin 80mg/placebo). Whole-night vPSG was conducted during the run-in and at the end of the treatment period. Videos of all rapid eye movement (REM) sleep periods were analysed for RBD behaviors (movements and vocalizations) using the Innsbruck classification system by two of the central reviewers, and a third reviewer adjudicated ambiguous cases.
Results: 34 patients (n=26 DLB, n=8 PDD; 85.3% men; mean age 71.3±6.36 years) were included in the analyses. Two (5.9%) patients were excluded due to protocol deviation in treatment compliance. Systematic video analysis demonstrated no difference between nelotanserin and placebo in RBD events. Bland–Altman plot showed high interrater reliability.
Conclusion: Despite negative results, this is the 1st randomized, placebo-controlled study on symptomatic RBD treatment using objective outcome measures based on systematic video analysis. This study provides a new method for outcome research in RBD and proves that movement analysis is a feasible and meaningful outcome for studies evaluating changes in RBD severity.
Disclosure: Support for research from Axovant

EPR-349

Sleep onset latency and sleep duration in adolescents with Internet addiction: the school-based study

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Background and aims: Accumulating evidence has shown that excessive Internet use is associated with a broad range of psychopathologic (depression, anxiety, and hyperactivity) and psychosomatic conditions, including sleep disturbances. Nighttime sleep onset latency and sleep duration are common sleep characteristics associated with social behavior patterns and psychological disorders. We aimed to evaluate the association of Internet addiction with these sleep characteristics in Siberian adolescents.

Methods: 4344 urban Siberian (Krasnoyarsk, Abakan, Kyzyl) school-based adolescents (aged 12–18) were tested with Chen Internet Addiction Scale (CIAS). Based on the CIAS, score Internet users were categorized into three groups: adaptive Internet users (AIU, scoring 27–42, n=2,237); maladaptive Internet users (MIU, scoring 43–64, n=1,799), and pathological Internet users (PIU, scoring 65, 308). Adolescents were asked "During the past month, how long (in minutes) has it usually taken you to fall asleep each night?" to estimate sleep onset latency. Bedtime and wake-up time on school days were assessed with the question: "At what times (hours:minutes) do you usually go to bed and wake up on school days?". Data are shown as median (25–75% quartiles). Kruskal-Wallis test was used.

Results: Sleep onset latency was notably increased in MIU and PIU groups in comparison with AIU group (Fig.1, p(Kruskal-Wallis test)<0.001). Opposite, sleep duration was progressively decreased with Internet addiction level (Fig.2, p(Kruskal-Wallis test)<0.001).

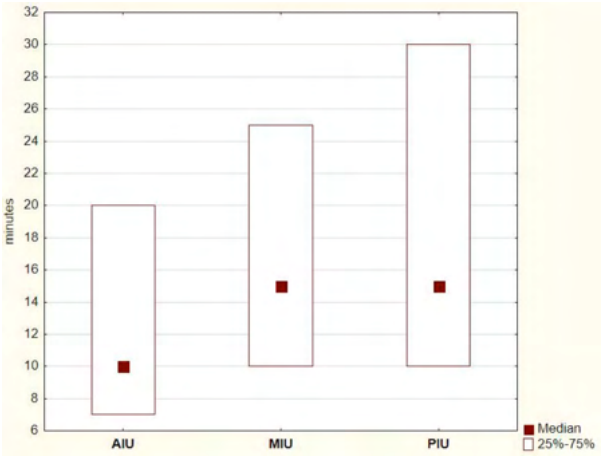

Figure 1. Sleep onset latency (in minutes) in in adolescents grouped according to CIAS score.

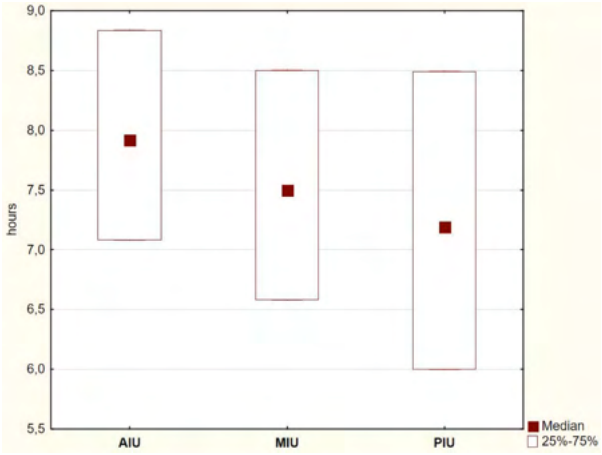

Figure 2. Sleep duration (in hours) in in adolescents grouped according to CIAS score.

Conclusion: We suppose that sleep disturbances in Internet-addicted adolescents may be explained by the higher rate of night activity and common pathogenic factors, such as personality characteristics, depression, anxiety.

Disclosure: We have nothing to disclose.

EPR-350

Pregnancy in narcolepsy

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Center for Narcolepsy, Clin. Sleep and Neuroimmunology, University Witten/Herdecke, Witten, Germany

Background and aims: Narcolepsy is a rare chronic brain disorder. First symptoms often occur in adolescence or young adults. Family planning and pregnancy are common and important subjects. We aimed at investigating characteristics, course of symptoms, and intake of medication before, during and after pregnancy.
Methods: Assessment was performed using an online survey tool. Women with narcolepsy and healthy women who gave birth to children were asked about their pregnancies. Data on demographics, socioeconomics, narcolepsy symptomatology, pregnancy and birth and on the child were assessed.
Results: Complete data from 38 patients with narcolepsy (79 aged-matched healthy controls) were analyzed. Mean age was 39.1 years for narcolepsy (39.2 for controls). During pregnancy, 52.6% of women with narcolepsy were working (mean 22h/week), versus 21.5% of controls. 23.6% of narcoleptics continued smoking during pregnancy (0% in controls). Symptoms of narcolepsy during pregnancy only slightly increased for EDS (moderate/severe EDS before pregnancy: 47.3%, before giving birth 60.5%) and maintained stable for cataplexy. There was an increase in number of naps/day (>1 nap per day: 21.1% vs. 55.3%) and duration of naps (mean 37 min vs. 72 min). Nocturnal sleeping became more frequent: 23.7% vs. 50% (weekly or more frequent episodes). Childbirth in narcolepsy was more often via caesarean section (34.2%) than in controls (16.5%). After giving birth most narcolepsy symptoms deteriorated (i.e. EDS, cataplexy).
Conclusion: Key symptoms of narcolepsy mainly maintain stable during pregnancy, but deteriorate after childbirth. The higher amount of working women during pregnancy indicate also for the socioeconomic burden of the disease.
Disclosure: I hereby declare, that I do not and have not had any business or personal relations to (industrial) companies or privately owned institutions, who would be relevant to the content of the presentation.

ePosters

Saturday, June 19 2021
Ageing and dementia 1

EPO-001

Delirium Screening in the Emergency Department

A. Akbari, B. Alam, Z. Khalil
Manchester, United Kingdom

Background and aims: Delirium is a common condition affecting one in eight acute hospital inpatients. Despite high prevalence and significant mortality rates, delirium remains a poorly detected condition. The non-specific symptoms of delirium make it difficult to detect, however, the Emergency Department (ED) at Salford Royal Hospital (SRH) introduced the 4AT tool to help detect delirium. Despite new tools and other efforts to increase the screening rate of delirium, they remain below target level (70%). This study aimed to identify reasons for poor screening rates and identify strategies to improve them to target level.
Methods: Surveys were conducted on staff in the ED, testing their knowledge of delirium and its screening methods. The results from the survey were compared to a previous study conducted in 2018, to see if there has been a change in the knowledge and use of delirium screening.

Survey on Delirium Assessment

This questionnaire is part of a project looking at recognition of delirium.

Ward:

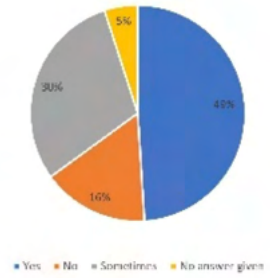
Job title: Nurse ANP Doctor: FY1/FY2 Registrar Consultant Other (please state):

1. Do you feel confident that you can diagnose delirium in a patient?
   Yes/No
2. Do you know any tool(s) that might be used to assess patients for delirium? What is it (are they) called?
3. Where do you find these tool(s)?
4. Do you use this tool to screen for delirium in those at risk? If not, why not?
   Yes/ Sometimes / No
5. Which form do you use to record the results of any tools used? Why?
6. What about a patient would cause you to screen for delirium?
7. What would you do if the delirium screening gave a positive result?
8. What causes of delirium are there?
9. Which patients are at high risk of delirium?
10. Has delirium screening been promoted? How?

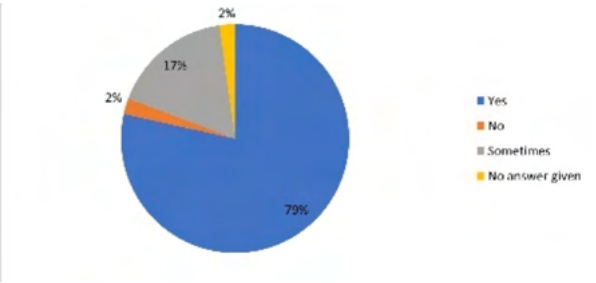
Contact: ahmed.ageed@student.manchester.ac.uk (University of Manchester 3rd year medical student)

The questionnaire utilised to collect data on the use of delirium screening among workers in the Emergency Department.

Results: There has been a regression in the knowledge of delirium screening from last year to this year's study. The recognition of the 4AT tool deployed at SRH decreased 30% from 2018 to 2019 among survey participants, despite it being on the admissions document for new patients. Among ED workers, consultants were found to be the worst at recognising the 4AT tool, whilst nurses were the best.



This figure demonstrates the responses from survey participants when asked whether they use the '4AT' tool to screen for delirium (2019)



This figure demonstrates the responses from survey participants when asked whether they use the '4AT' tool to screen for delirium (2018)

Conclusion: The rate of delirium screening at SRH has decreased over the last year. The main barrier to delirium screening highlighted in this study was knowledge of delirium screening itself. This suggests a strong need for increased teaching among workers in the ED on screening methods.
Disclosure: No conflicts of interest.

EPO-002

Neuromodulation to promote recovery in patients with disorders of consciousness: a systematic review and meta-analysis

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Background and aims: Therapeutic options for patients with disorders of consciousness (i.e. DOC) are still under-explored. Neuromodulation involves stimulating specific brain areas to alter neural activity and is considered a promising field for the treatment of patients with DOC.
Methods: We conducted a systematic review of publications using neuromodulation techniques as a tool to stimulate responsiveness in patients with DOC. Effect sizes of CRS-R changes and their confidence intervals were calculated using the Hedge's g formula. The studies were analyzed including all patients, then separately according to diagnosis and technique.
Results: 26 articles were included in the qualitative review (n =503, 255 F, 176 traumatic brain injury, 48.3±14.3 y.o., 26.2±33.5 months post injury). 12 studies used transcranial electric stimulation (tES), nine repetitive transcranial magnetic stimulation (rTMS), four spinal cord stimulation (SCS), one near-infrared low level laser therapy and one focused shock wave therapy. 19 studies used a standardized behavioural scale and 14 of them reported behavioural improvement after neuromodulation; however only 11 were significant. 11 studies were included in the meta-analysis (8 tES and three rTMS) and we found a significant effect size (ES: 0.67; CI: 0.44, 0.90). Effect sizes were significant also for each technique (tDCS ES: 0.66; CI: 0.36, 0.95; rTMS ES: 0.73; CI: 0.14). When taking into account diagnosis only tDCS on MCS patients was found significant (ES: 0.70; CI: 0.20, 1.21)

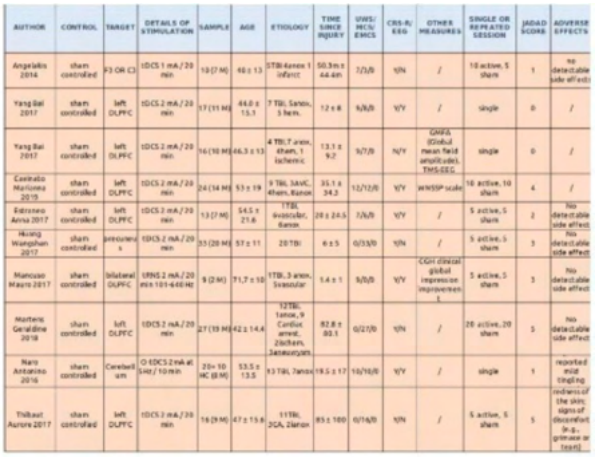

Table 1. Results of Qualitative analysis; specifics on included studies using tES.

Table 2. Results of Qualitative analysis; specifics on included studies using SCS in yellow, rTMS in green and N-LT/F-SWT in purple.

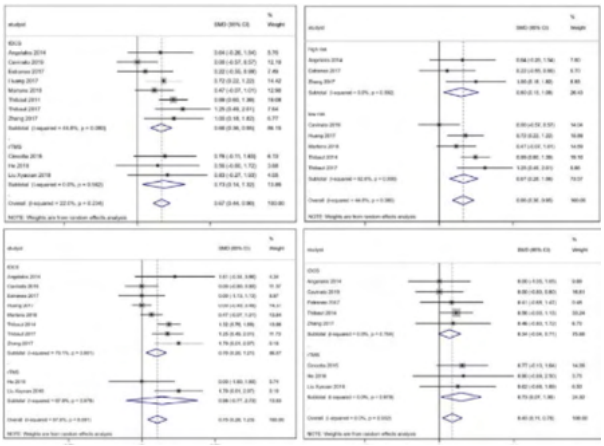

Table 3. Forest Plot of Metanalysis results. Top left: all studies on both tDCS and rTMS. Top right: all studies classified by risk of bias (i.e. low risk and high risk). Bottom left: UWS only. Bottom right: MCS only

Conclusion: This systematic review shows that neuromodulation is a worthwhile option for the treatment of patients with DOC. tES and rTMS have showed their efficacy in improving responsiveness.
Disclosure: The authors have nothing to disclose.

EPO-003

Montreal Cognitive Assessment in the Elderly Croatian Population

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Background and aims: The aim of the study was standardization and validation of the Montreal Cognitive Assessment (MoCA) test in the elderly Croatian population.
Methods: 253 participants were recruited in the study (107 without cognitive impairment and 146 with MCI). Among MCI subjects 35 were MCI-AD and 111 were diagnosed scVCI-ND.
Results: The optimal cutoff point for screening of the general Croatian population (cognitively healthy vs. MCI) in subjects 45 years was 26/27 with the sensitivity of 90.1% and low specificity (40.4%) and in subjects 65 years was 23/24 with low specificity as well (55.6%). When including only subjects 65 years with a higher/university education completed (14 years of education) the cutoff point was 26/27 with the best sensitivity and specificity (93.1% and 90.0% respectively). Additionally, when including subjects 45 years with 12 years of education the cutoff point was 26/27 with sensitivity of 85.5% and specificity of 88.1%. Unlike highly educated subjects, the optimal cutoff point was very low (18/19) for subjects with eight years of education or less with low specificity.
Conclusion: Only in groups of highly educated subjects (at least 12 years of education) ideal sensitivities and specificities were found.
Disclosure: The authors report no conflict of interest.

EPO-004

Asymmetric rapidly progressive idiopathic normal pressure hydrocephalus: description of a case

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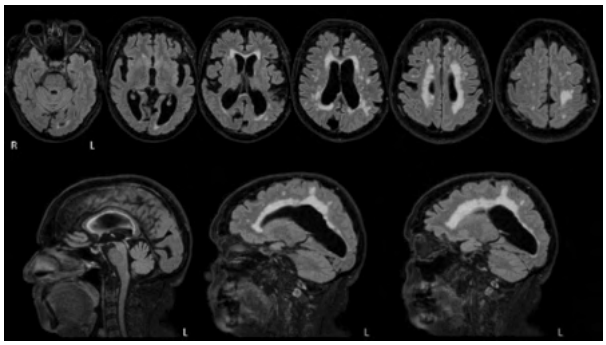
Background and aims: Idiopathic normal-pressure hydrocephalus (INPH) diagnosis is sometimes tricky in presence of atypical clinical/neuroimaging manifestations.
Methods: A 76-year-old woman was hospitalized referring 2-months history of instability, poor concentration and urinary urgency with insidious onset and significant worsening in the last week. Her history was notable for essential tremor, anxious syndrome, moderate scoliosis and hypertension.
Results: On admission, she showed mild attentive-executive deficits and right-sided mixed hypertonia, right-more-than-left postural and kinetic tremor and inconstant dystonic posture of right upper limb. She exhibited wide-based gait with postural instability. Brain MRI revealed asymmetric left-more-than-right ventriculomegaly with severe leukoencephalopathy involving extensively the corpus callosum and the white matter from ventricular tegmentum until semioval centers reaching the subcortical motor areas on the left side, and cortical atrophy. Cerebrospinal fluid (CSF) tap-test lead to minimum improvement of clinical picture for few hours. CSF pressure was normal. Research on CSF of infectious agents, onconeural antibodies, malignant cells and degeneration biomarkers was negative. She continued to worse becoming in two weeks markedly confuse, bedridden with severe right hypertonic-dystonic hemisyndrome. MRI showed a minimum increase of ventriculomegaly and of leukoencephalopathy. Hypothesizing an atypical INPH, we made the patient undergo ventriculo-peritoneal shunting. After surgery, the patient progressively improved. In one month, she recovered limb motor function, she was able to use walker for short distances, and her cognitive status returned to pre-morbid condition.



MRI findings. Axial and sagittal FLAIR sequences displayed asymmetric ventriculomegaly, severe leukoencephalopathy and moderate cortical atrophy. Images are shown in radiological convention (right is left).

Conclusion: INPH atypical picture in older patients might be due to overlapped pre-existing neurological comorbidities and/or brain abnormalities such as atrophy or vascular lesions.
Disclosure: Filippi:Editor-in-Chief JOON;compensation for consulting/speaking activities/research support from Bayer-Biogen Idec-Merck-Serono-Novartis-Roche-Sanofi Genzyme-Takeda-Teva PI; research support from Italian Ministry of Health, FISM,ARiSLA

EPO-005

Atypical development of neurosyphilis: a complex clinical and imaging picture

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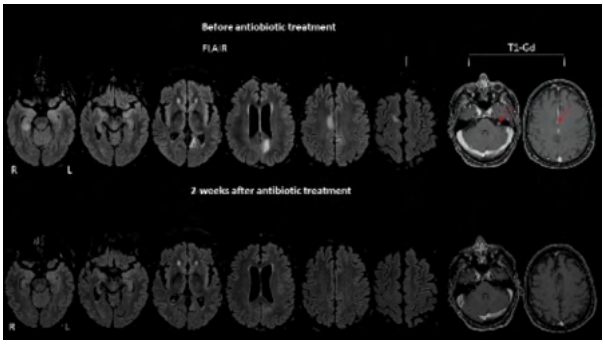
Background and aims: Symptomatic neurosyphilis is characterized by a wide spectrum of clinical and imaging features that can make diagnosis challenging.
Methods: We admitted to our Neurology Unit a 59-year-old man with 1-month history of progressive movement and cognitive impairment. An outpatient brain MRI performed two weeks after onset was negative.
Results: On neurological examination, the patient showed moderate cognitive impairment with poor insight and disinhibition, truncal and gait ataxia, and postural and kinetic tremor limb tremor. He repeated brain MRI (day-30) showing multifocal bilateral hyperintensities mainly in mesial-temporal and cingular cortex and a long-T2 nodular signal shadow, with a diameter approximately 5–6 mm, adjacent to the superior border of left petrous temporal bone, near the free margin of tentorium, enhanced after gadolinium injection. Lumbar puncture showed inflammatory cerebrospinal fluid (CSF) with 29 cells/microliter and protein level of 88mg/microliter (normal 12–60) and normal glucose. Search for viral agents and bacterial culture were negative. Serum HIV testing was negative. CSF and serum panel for onconeural antibodies was negative. The patient showed blood and CSF positive TPHA, positive CSF FTA-abs, elevated CSF anti-treponema IgG-index of 13.8 (normal <1.3) suggestive for intrathecal synthesis. Based on clinical, biological and neuroimaging data the patient was diagnosed with neurosyphilis. He was treated with a 2-week course of penicillin with a dramatic clinical and neuro-imaging improvement.



Axial FLAIR and T1 post-gadolinium (T1-Gd) sequences displayed brain alterations before (top picture) e after two weeks of antibiotic treatment (bottom picture). Images are shown in radiological convention (right is left).

Conclusion: Despite neurosyphilis being an uncommon cause of rapidly progressive cognitive-movement disorders, it should be always considered in the differential diagnosis with other inflammatory or neurodegenerative diseases.
Disclosure: Filippi:Editor-in-Chief JOON;compensation for consulting/speaking activities/research support from Bayer-Biogen Idec-Merck-Serono-Novartis-Roche-Sanofi/ Genzyme-Takeda-Teva PI; research support from Italian Ministry of Health, FISM,ARiSLA

EPO-006

Gait impairments and functional limitations in the exploratory activity in an animal model of Alzheimer's disease

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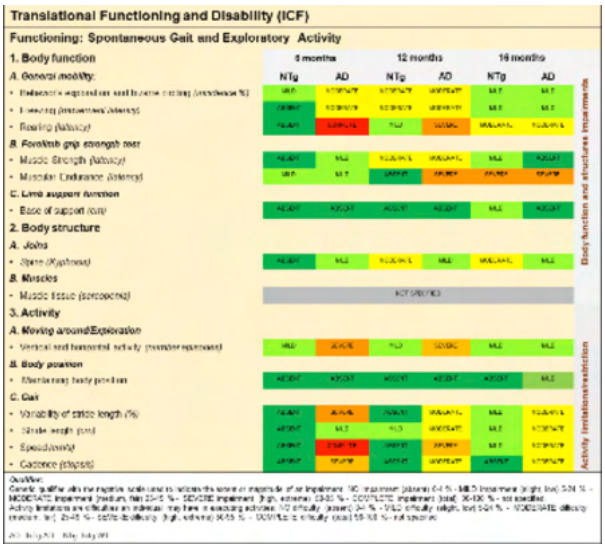
Department of Psychiatry and Forensic Medicine, School of Medicine, Universitat Autònoma de Barcelona, Barcelona, Spain

Background and aims: Gait impairments in Alzheimer's disease (AD) result from structural and functional deficiencies that generate limitations in the performance of activities and restrictions in an individual's biopsychosocial participation. In a translational way, we have used the conceptual framework proposed by the International Classification of Disability and Health Functioning (ICF) to classify and describe the functioning and disability on gait and exploratory activity in the 3xTg-AD animal model.
Methods: We developed a behavioral observation method that allows us to differentiate qualitative parameters of psychomotor performance in animals' gait, similar to the behavioral patterns observed in humans. The functional psychomotor evaluation allows measuring various dimensions of gait and exploratory activity at different disease progression stages in dichotomy with aging. We included male 3xTg-AD mice and their non-transgenic counterpart (NTg) of 6, 12, and 16 months (n=45).
Results: Here we present the preliminary results. The 3xTg-AD mice show more significant functional impairment in gait and exploratory activity quantitative variables. The presence of movement limitations and muscle weakness mark the functional decline related to the disease severity stages that intensify with increasing age. Motor performance in 3xTg-AD is accompanied by a series of bizarre behaviors that interfere with the trajectory, which allows us to infer poor neurological control. Besides, signs of physical frailty accompany the functional deterioration of these animals.



Gait impairments and functional limitations in the exploratory activity: Translational approach of Functioning and Disability

Conclusion: The use of the ICF as a conceptual framework allows the functional status to be described, facilitating its interpretation and application in the rehabilitation of people with AD.
Disclosure: Nothing to disclose.

EPO-007

Hindlimb clasping, kyphosis and piloerection: Frailty markers from middle to very old ages in mice

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Background and aims: The state of frailty is a clinical-biological syndrome that affects the elderly population with a higher risk of functional dependence. It is produced by the dysfunction of multiple organs and systems, causing a significant hospitalization, disability, and death rate. However, individual variability increases with the aging process, and divergence between chronological and biological age becomes more prominent. This research aims to identify distinctive aspects of physical frailty, from a behavioral neurology translational approach.

Methods: The animal model 3xTg-AD for Alzheimer's disease (n=37) and its non-transgenic (NTg) counterpart with normal aging (n=14), from 12 to 21 months modeling middle-age to very-old scenarios, were used. The animals' functional limitations and impairments were assessed to define their Physical Frailty Phenotype. The classical open-field anxiety test was included to control for general horizontal and vertical activities.

Results: We have detected common elements of physical frailty and functional performance in all the animals, independently of their genotypes and age. Signs such as piloerection, kyphosis, and hindlimb clasping seemed to be the ones that better defined the level of severity and deterioration, as confirmed by end-of-life scenarios. They are important to note since they may influence the other physical and behavioral results.

Physical Frailty Phenotype	NTg N=14	3xTg-AD N=37	Statistics
Body position	-	6/37 (16%)	n.s.
Kyphosis	14/14 (100%)	35/37 (95%)	n.s.
Alopecia	4/14 (29%)	6/37 (16%)	n.s.
Palpebral closure	2/14 (14%)	4/37 (11%)	n.s.
Piloerection	11/14 (79%)	28/37 (76%)	n.s.
Tail position	-	4/37 (11%)	n.s.
Tremor	2/14 (14%)	12/37 (32%)	n.s.
Hindlimb clasping:			
• *Normal*	5/14 (36%)	10/37 (27%)	n.s.
• *Mild*	7/14 (50%)	20/37 (54%)	n.s.
• *Moderate*	2/14 (14%)	6/37 (16%)	n.s.
• *Severe*	-	1/37 (3%)	n.s.
X_2 *** p < 0.01, ** p < 0.05 * p < 0.05, n.s. p > 0.05			

Table 1. Physical Frailty Phenotype

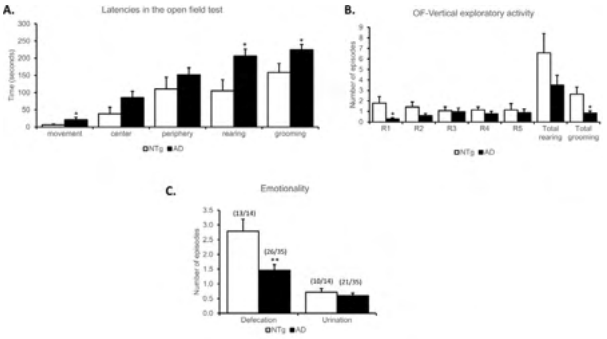

Figure 1. Ethogram in the Open Field test (OF)

Conclusion: Inter-individual heterogeneity from the middle to ancient age can disrupt the relationship between chronological age and animals' physical status/frailty. Identifying markers of frailty independent of chronological age may help us translate them into clinical settings and better design interventions in the frailest population with normal and/or neuropathological aging.

Disclosure: Nothing to disclose.

EPO-008

Sleep quality in Romanian PD patients during COVID-19 pandemic

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Background and aims: COVID-19 pandemic has serious consequences on general and mental health. The restrictive measures that were proposed in attempt to reduce the spread of the virus were also found to impact various aspects of quality of life. Objectives: To identify if the lockdown period imposed in the context of COVID-19 pandemic has any consequences on sleep quality among Parkinson's disease (PD) patients in Romania.
Methods: Prospective online survey on 134 PD patients from the whole Romania. The online survey included items regarding socio-demographic data, various questions related to sleep disorders, standardized rating tools for sleep assessment – Parkinson's Disease Sleep Scale-2 (PDSS-2) and SCOPA sleep.
Results: There were 74 men (55%), mean age 61.3±5.42 years. Most patients (68.65%) reported a global worsening of the sleep quality during lockdown comparing to baseline. The most common consequences of the sleep disturbances that occurred during the lockdown were fatigue (59.7%), concentrating difficulties (47.8%), anxiety (35%) and depression (27.6%). According to the patients' opinion, the most common reasons why these sleep disturbances occurred during lockdown were the persistent feelings of fear (44.7%), worrisome thoughts (39.5%) and the lack of physical activity (38.8%). Some patients (31.3%) started to use sleep medication to treat the sleep disturbances that occurred/worsened during the quarantine period.
Conclusion: The lockdown measures imposed in the context of COVID-19 pandemic had important negative consequences on quality of sleep in PD patients.
Disclosure: Nothing to disclose.

EPO-009

Ultra-Deep Proteomic Profiling of Cerebrospinal Fluid for Unbiased AD Biomarker Discovery and Subject Stratification

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Zurich, Switzerland

Background and aims: Cerebrospinal fluid (CSF) is established as a key matrix that enables interrogation of biological processes within the central nervous system. CSF biomarkers may support development of new therapies through patient stratification, determining prognosis or disease aggressiveness, and response monitoring. Here, we seek to address this unmet need by applying a novel discovery workflow, based on high field asymmetric waveform ion mobility spectrometry (FAIMS) coupled to data-independent acquisition mass spectrometry (DIA-MS).
Methods: CSF samples were obtained from subjects with late onset Alzheimer's disease (LOAD; n=16) and age-matched normal controls (CO; n=8). Quantification was performed with FAIMS-DIA-MS setup using 4h gradients. DIA data analysis was performed using Spectronaut (Biognosys). Peptide and protein false discovery rate was set to 1%.
Results: Across all samples 3,473 proteins were identified and quantified. The pool of quantified proteins comprises well characterized species associated with AD and other neurological disorders such as BACE1, APP, MAPT (Tau), SNCA, NFL, NFH and NFM. Moreover, the depth and breadth of protein quantification covers numerous pathological mechanisms such as AB and Tau pathology, synaptic dysfunction (e.g. SPTX2 and SNAP25), neuronal injury, iron toxicity and inflammation.
Conclusion: The FAIMS-DIA-MS workflow is scalable to the profiling of 1,000s of samples and can thus be applied for subject stratification and biomarker discovery in clinical cohorts. We envision the unbiased quantification of >3,000 proteins in CSF to aid the discovery of new AD biomarkers as well as the elucidation of complex disease mechanisms.
Disclosure: All authors are employees of Biognosys AG.

EPO-010

Photosensitive epilepsy and polycystic ovary syndrome as manifestations of MERRF

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Background and aims: Though endocrinologic involvement and epilepsy are frequent features of myoclonic epilepsy with ragged-red fibers (MERRF), polycystic ovary syndrome (PCOS) and photosensitive epilepsy have not been reported.
Methods: Case report
Results: A 32 yo female was diagnosed with MERRF at age 19y upon presence of the four canonical features and the variant m.8,344A>G in MT-TK (tRNA(Lys)) (blood heteroplasmy rate: 50%). She experienced recurrent photosensitive focal and generalised seizures since age 19y, which could be triggered by flickering light or by looking at small stones, leaves, or dirty snow on the ground. Since the last 42 months she was seizure-free upon levetiracetam (4000mg/d), clonazepam (1.5mg/d), and topiramate (25mg/d). Additionally, she suffered from secondary amenorrhoea since adolescence. She was married between ages 19y and 25y but did not get pregnant. PCOS was diagnosed and treated with desogestrel plus estradiol. Nonetheless the course was progressive, particularly with regard to ataxia, myocloni, and myopathy.
Conclusion: The phenotypic spectrum of MERRF is broader than anticipated and may additionally include PCOS and photosensitive epilepsy. PCOS in MERRF may respond to hormone substitution and photosensitive epilepsy to levetiracetam, clonazepam, and topiramate.
Disclosure: Nothing to disclose.

EPO-011

Mean cost of hospitalizations by Parkinson's disease in the Brazilian public health system per region between 2009–2019

B. Franco [1], D. Miranda [1], G. Aragão [1], F. De Jesus [1], C. Filho [1], L. Cordeiro Magalhães [1], M. Cotrim Pereira [2], M. Weber [1], I. Mascarenhas de Andrade [2], B. Silveira [1], N. Farias [1]
[1] *Salvador, Brazil,* [2] *Salvador-Bahia, Brazil*

Background and aims: Parkinson's disease (PD) has a high prevalence worldwide. However, its cost on a national light is unclear. The study aims to inspect the cost of hospitalizations by PD in Brazilian public health between 2009–2019.
Methods: In this descriptive observational ecological study, we studied the mean cost of hospitalizations by PD per patient, in Brazillian Real, per treatment location in 2009–2019. Data was collected through the Informatic Department of the Brazilian Unified Health System. We used measures of dispersion and central tendency.
Results: Nationwide, the year with the highest mean cost was 2019 (mean=3432.636; SD=2242.4; 95% CI=1,467.11–5,398.16) and the lowest was 2012 (mean=917.97; SD=736.76; 95% CI=272.18–1,563.76). The annual growth rate was 9.6% per year. The Southeast had the highest mean cost (mea=3,564.22; SD=1,234.02; 95% CI=2,834.97–4,293.47), while the North had the lowest (mean=607.26; SD=367.36; 95% CI=390.17–824.35). The 2nd highest mean cost was of the South (mean=2,268.36; SD=1,581.08; 95% CI=1,334.02–3,202.70), followed by the Center-West (mean=1,479.41; SD=1,579.02; 95% CI=546.28–2,412.54) and the Northeast (mean=1,386.65; SD=457.33; 95% CI=1,116.33–1,656.91).
Conclusion: Disparities in the cost of admissions by PD across Brazil reflect unconformities regarding life expectancy, access to healthcare, and demographic density. More studies are needed to expand this investigation.
Disclosure: The authors have no conflict of interest.

EPO-012

Economical impact of hospitalizations by Alzheimer's disease in the Brazilian public health system

B. Franco [1], D. Miranda [1], G. Aragão [1], F. De Jesus [1], C. Filho [1], N. Farias [1], B. Silveira [1], I. Mascarenhas de Andrade[2], L. Cordeiro Magalhães[1], M. Cotrim Pereira [2], M. Weber [1]
[1] Salvador, Brazil, [2] Salvador-Bahia, Brazil

Background and aims: Alzheimer's disease (AD) is the most prevalent neurodegenerative disease worldwide. Therefore, it is relevant to assess the economic burden of admissions by AD at a national level, measuring its costs to society across different regions of the country.
Methods: In this descriptive observational ecological study, we collected data upon AD inpatient treatment across Brazilian regions where patients received care, between 2009 and 2019. Data was gathered through the Informatic Department of the Brazilian Unified Health System (DATASUS) in Brazilian coin. Statistical analysis was based on measures of dispersion and central tendency.
Results: The highest mean cost values of hospitalization correspond to the Southeast region (mean=2,532,8; SD= 974,4; 95% CI=1,957,0–3,108,6) and the lowest to the North region (mean=480,1; SD=126,4; 95% CI=405,5–554,9). Nationwide, the year with the highest total hospitalization value was 2014 (mean=558.063,1; SD= 1.004.456,0; 95% CI=-322.365,31–143.8491,4) and the lowest was 2011 (mean=278.243,7; SD=443.503,1; 95% CI=-110.496,8–666.984,1).The year with the highest number of hospitalizations was 2017 (mean=320,2 SD=365; 95% CI=0,23–640,16) and the lowest was 2009 (mean=141,8 SD=166,4; 95% CI=-4,1–287,7).
Conclusion: The Southwest region stood out by holding the highest total and mean expense of hospitalizations, and highest number of admissions. The opposite occurred in the North. These results reflect Brazilian disparity in life expectancy, access to healthcare, and demographic density. Additional studies are necessary to deepen this investigation.
Disclosure: The authors have no conflicts of interest.

EPO-013

Cognitive impairment detected by MoCA (Montreal Cognitive Assessment) test after COVID-19 in Mexico

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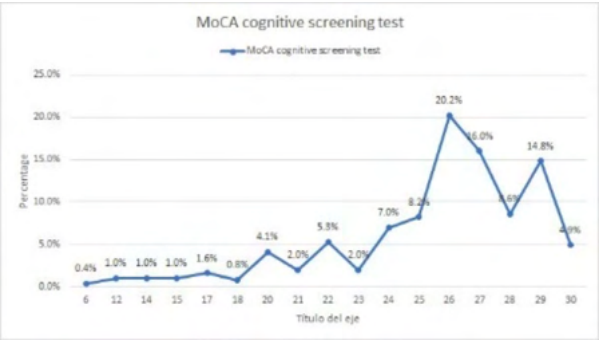
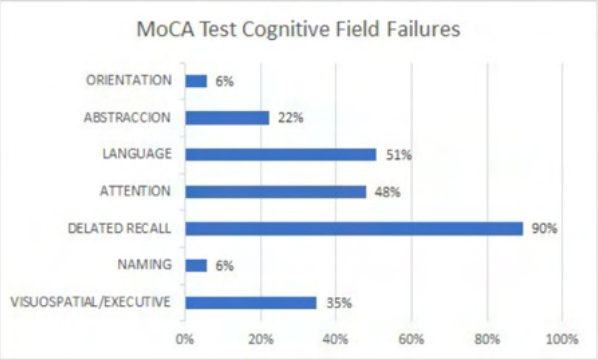
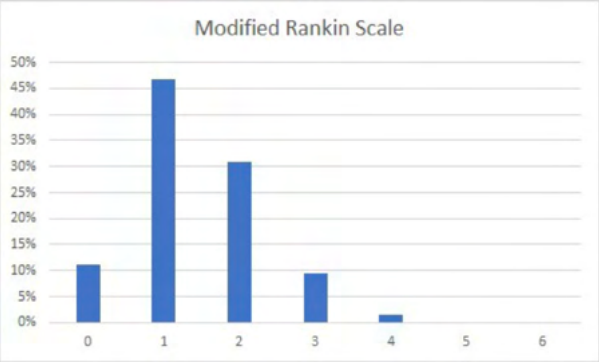
Background and aims: The year 2020 was marked by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic, that causes the human coronavirus disease 2019 (COVID-19). Multiple neurological symptoms have been reported; however, there is scarce knowledge about their impact on cognitive functions in recovered patients.
Methods: We report the results of the MoCA cognitive screening test (Mexican Version 7.3), applied by two neurologists to 242 patients who were admitted at a single medical center in Mexico City with acute respiratory distress syndrome (ARDS) due to COVID-19, three months after their hospital discharge, from August 31, 2020 to January 11, 2021.
Results: All patients were positive for SARS-CoV-2, tested via reverse-transcriptase-polymerase-chain-reaction (RT-PCR) assays of nasopharyngeal samples. The mean age of the cohort was 52 years, 145 patients (59.9%) reported cognitive imparment by themselves or by their relatives. 171 (70.6%) patients had fewer than 12 years of schooling; three patients already had previous cognitive complaints; bradykinesia was found in two patients. The average score on the MoCA test was 25.5; 37 patients scored between 22 and 14 points, and four patients scored less than 12 points. We requested brain magnetic resonance imaging and neuropsychological tests to all patients with cognitive complaint or with MoCA scores under 23 points. These studies are still in progress.



MoCA test scores of the 238 patients evaluated three months after discharge



Specific field failures found in the MoCA test of all patients evaluated within three months of their hospital discharge



Percentages in category on the modified rankin scale three months after discharge

Conclusion: Neurological manifestations in pandemics frequently cause long-term consequences which are frequently overlooked. The cognitive impairments found in the MoCA sreeening test in COVID-19 survivors may have a multifactorial origin, yet requires further evaluations and close long-term follow-up.
Disclosure: Nothing to disclose.

EPO-014

Factors associated with diagnostic delay in patients with Frontotemporal Lobar Degeneration

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Background and aims: Despite recent advances in the characterization of Frontotemporal Lobar Degeneration (FTLD), its early diagnosis remains a challenge and depends in the first place on the consultation delay and then on the diagnostic delay. The objective was to compare 1) consultation and diagnostic delays within the spectrum of FTLD, and 2) to study the factors associated with their lengthening in the behavioral variant FTD population (bv-FTD).
Methods: From the regional MEOTIS datase were selected the patients who consulted at the Lille memory center between 2000 and 2016 and for whom a diagnosis of FTLD was made. Patients were sorted according to their initial clinical presentation: behavioral, language (lv-FDT) or motor (m-FDT). We collected the age at onset of first symptoms and the dates of first visit and of diagnosis in order to calculate consultation and diagnostic delays.
Results: 349 patients were included: 184 bv-FTD, 78 lv-FDT et 87 m-FTD. The consultation delay ranged from 35.6 to 41 months with no significant difference depending on the presentation ($p=0.855$) and the diagnostic delay ranged from 13.4 to 22.7 months. For bv-FDT patients, the younger the patients, the longer was the consultation delay ($p<0.001$). The diagnosis delay was longer in patients with a psychiatric history ($p=0.012$) or vascular risk factors ($p<0.001$).
Conclusion: The consultation delay was the main factor delaying appropriate care, especially for the youngest DFT patients and one of the challenges is to differentiate them from psychiatric diseases. These findings call for increased attention to the signs of the FTD disorders.
Disclosure: I do not have any conflict of interests to report.

Cerebrovascular diseases 1

EPO-015

Cerebral hyperperfusion syndrome with epileptic seizures after carotid revascularization: a case report

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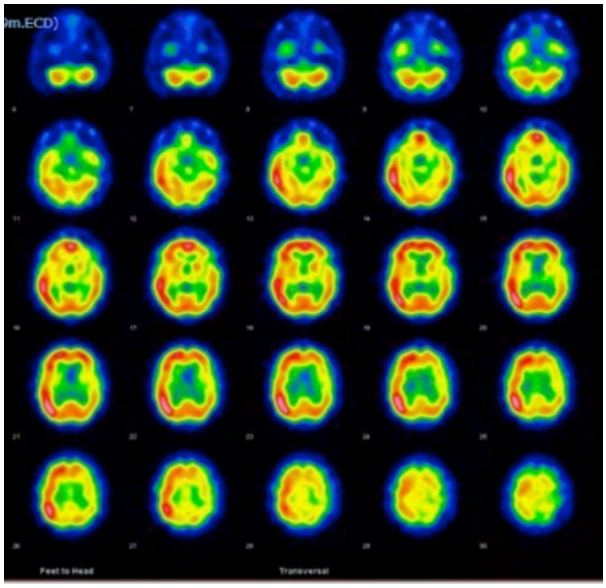
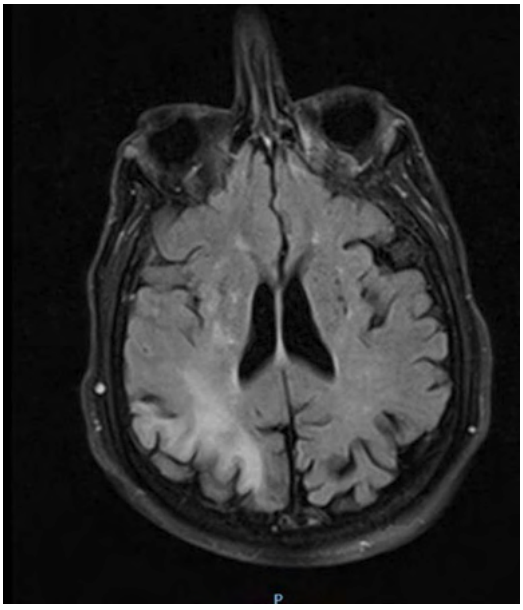
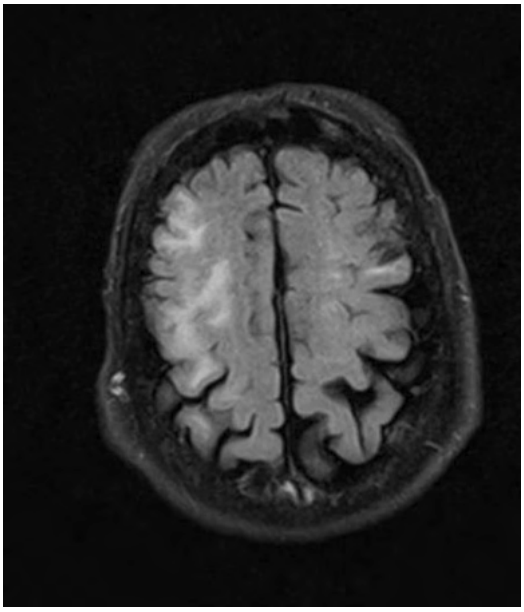
Background and aims: Reperfusion syndrome, despite being a very rare complication (0-3%), entails high morbimortality. The usual symptomatology consists of severe ipsilateral headache, eye and facial pain and focal neurological deficits. However, epileptic seizures are rare. We present a rare case to reperfusion syndrome with sintomatic epileptic seizure confirmed with functional brain imaging tests.
Methods: Case report
Results: A 65-year-old patient underwent right carotid endarterectomy. four days later he presented acutely myoclonus on the left side face and left arm, inexhaustible and maintained with postural changes. In addition, he presented left facial paralysis, left hemianopia, dysarthria and left babinski. Blood pressure after the intervention remained normal. Head CT did not show acute lesions. CT angiography showed a penetrating ulcer in the right common carotid artery. MRI showed a hyperintensity in T2 and FLAIR sequences. In the EEG showed periodic lateralized epileptiform discharges more evident in the right hemisphere. The study was completed with SPECT, who showed a peculiar image of homogeneously increased perfusion in the right hemisphere with respect to the contralateral side. This finding confirmed the clinical suspicion: symptomatic focal seizures secondary to reperfusion-hyperperfusion syndrome after carotid revascularization.



SPECT



MRI (T2)



MRI (T2)

Conclusion: This case is one of the rare cases of epileptic seizures in patients with cerebral hyperperfusion syndrome after endarterectomy evidenced by functional imaging tests. The pathophysiology is not fully understood, but a problem in the autoregulation of cerebral flow in patients with chronic vascular damage is postulated as the main cause. However, more studies are needed.
Disclosure: Nothing to disclose.

EPO-016

Assessment of mortality risk in Covid-19 patients with ischemic cerebrovascular disease

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Background and aims: Covid-19 associated cerebrovascular complications have been frequently reported. There are many publications about the risk of developing cerebrovascular disease (CVD) during or after Covid-19. In this study, factors affecting mortality in patients with ischemic CVD during or after Covid-19 were investigated.
Methods: For this purpose, data of 20 Covid-19 patients who were diagnosed with ischemic CVD during hospitalization were retrospectively analyzed and correlation analyzes were performed.
Results: 70% of the patients had hypertension, 50% had diabetes, 45% had cardiac disease, 20% had a history of CVD. Hypercoagulability was detected in 85%. Ischemic involvement in multi-vessel areas was observed in 60%. Mortality rate after CVD was 55%. There was no significant correlation between mortality and gender, hypertension, diabetes, cardiac disease, or previous cerebrovascular disease. Prophylactic anticoagulant was started after Covid-19 was detected in all patients evaluated. No significant correlation was observed between antiaggregant or anticoagulant use and mortality. Mortality was found to be statistically significantly higher in patients with ischemia in the multivessel area (p=0.028). It was found that the NIH scores of those who had ischemic CVD between 12–25 days of Covid-19, were statistically significantly higher (p=0.031).
Conclusion: In this report, factors affecting mortality in patients with coexistence of Covid-19 and ischemic CVD were investigated. Mortality is higher in ischemia affecting multi vessel areas. Clinical findings are more severe in people who had ischemic CVD after 12. day of Covid-19. It is possible to associate this finding with the emergence of cytokine storm at a later stage of the infection.
Disclosure: No conflict of interest.

EPO-017

Complications related to mechanical thrombectomy in acute ischemic stroke patients

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Background and aims: It has been proven by randomized controlled studies that mechanical thrombectomy is effective and safe in acute ischemic stroke patients presenting with major vessel occlusion. Periprosedural and post-procedural complications could be seen due to mechanical thrombectomy. In our study, we aimed to present the complications and effects we experienced in patients who underwent mechanical thrombectomy.
Methods: Total 384 patients underwent mechanical thrombectomy with the diagnosis of anterior system acute ischemic stroke due to major vessel occlusion were retrospectively identified. Relevant clinical data and risk factors were collected.
Results: A total of 384 patients with a mean age of 62.21± 13.45 were included in the study. A total of 167 (43.8%) patients were given thrombolytic therapy. Access site related, intracranial bleeding, iatrogenic vessel dissection, vessel rupture, new territorial embolism, distal embolism, reoclusion, vasospasm were identified complications due to mechanical thrombectomy (Table). Successful recanalization (TICI 2b–3) was achieved in 83% of patients (n=319). The mRS value of 57% of our patients (n=219) at the 3rd month was between 0–2.

Table : Complications

Access site related (femoral puncture)	Embolectomy	5
	Pseudoaneurysm	2
	Hematoma	1
Intracranial Bleeding	%27.6 (n=106)	
Iatrogenic vessel dissection	%0.05 (n=20)	
Vessel rupture	%0.01 (n=6)	
New territorial embolism	%0.03 (n=12)	
Distal embolism	%53.9 (n=207)	
Reocclusion	%0.05 (n=21)	
Vasospasm	%28.3 (n=109)	

Conclusion: Complications related to mechanical thrombectomy can be seen during and after the procedure and can reduce the survival of patients and extend the rehabilitation period. Hence, early recognition of complications at the right time and effective treatment will reduce poor clinical outcomes and mortality rates.
Disclosure: The authors declares that they have no conflict of interests. There are no financial relationships to disclose.

EPO-018

Impact of thrombocytopenia on the safety and efficacy in patients treated with mechanical thrombectomy

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Background and aims: Platelet counts have been recognized as an independent predictor of outcome in patients with acute ischemic stroke (AIS) or transient ischemic attack. The aim of our study was to determine the impact of thrombocytopenia on the safety and efficacy of endovascular thrombectomy (ET) in patients with AIS due to anterior circulation large vessel occlusion (LVO).
Methods: In this study, 129 consecutive patients with AIS due to anterior LVO who underwent ET during a 2-year period were included. The primary safety outcome was symptomatic intracerebral hemorrhage (SICH), while the secondary safety outcome was stroke-related mortality. The efficacy outcome was functional independence, defined as a modified Rankin Scale (mRS) score 0–2. The follow-up period was 90 days. The patients were divided into two groups based on initial platelet count: with thrombocytopenia (<150x109/L) and without thrombocytopenia (150x109/L).
Results: Initial thrombocytopenia was detected in 19 (15%) patients. There was no difference in the presence of SICH between these two groups. Mortality was higher in patients with thrombocytopenia (47.4% vs. 22.2%, p=0.043). Moreover, it was detected as an independent predictor of short-term mortality (aOR 6.75, 95% CI 1.49–30.65, p= 0.013). The main cause of death in the group with thrombocytopenia was malignant cerebral infarction (44.4%). There was no difference in the percentage of functionally independent patients three months after ET.
Conclusion: Initial thrombocytopenia is an independent predictor of short-term mortality in patients with AIS due to anterior LVO who underwent ET.
Disclosure: Nothing to disclose.

EPO-019

Cryptogenic Ischemic Stroke Secondary to Carotid Web

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Background and aims: The Carotid web (CW) represents a rare and under-recognized potential source of cerebral emboli. Understanding the pathogenesis and the typical imaging features of CW, and accurately diagnosing the CW will help to implement targeted intervention for cryptogenic stroke and reduce the recurrence of stroke events. We aimed to explore clinical and imaging features of the CW in patients with cryptogenic stroke, to assess the rate of stroke recurrence and to underline the interest of carotid stenting in secondary prevention.
Methods: The clinical data of five patients who were admitted to Neurology department for a cryptogenic stroke and were then diagnosed with CW were retrospectively reviewed. All patients benefited of rigorous clinical examination, cardiac evaluation, intracranial and neck vessel imaging (CT-angiography or arteriography), and regular follow-up.
Results: The mean age was 47 (30–52) years, a sex ratio (H/F) of 0,25. Rigorous cardiac evaluation did not reveal any abnormalities. CT-angiography of the neck vessels confirmed the diagnosis of CW in 60% of patients, however arteriography was necessary in 40% to confirm the diagnosis. There were no patients with bilateral webs. A recurrent stroke/transient ischemic attack (TIA) involving the territory of the previously symptomaic web occurred in % patients (4strokes/1TIA). Foor recurrences occurred on dual antiplatelet therapy and one off antithrombotics. 80% of patients were stented with no periprocedural complications. No recurred strokes/TIAs occurred in stented individuals.
Conclusion: Carotid web is associated with high recurrent stroke/TIA risk, despite antithrombotic use, and is amenable to carotid stenting.
Disclosure: Nothing to disclose.

EPO-020

Cryptogenic ischemic stroke: carotid web, a case series

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[1] Madrid, Spain, [2] Neurology, Madrid, Spain

Background and aims: Carotid web is an underdiagnosed etiology of recurrent embolic stroke, usually affecting young patients with few vascular risk factors. Optimal management strategies for secondary prevention remain unclear. There is no evidence on anticoagulation, and while single antiplatelet therapy seems insufficient, temporary dual antiplatelet therapy may be considered an option. Recent studies suggest that carotid artery stenting and carotid endarterectomy are safe and effective.
Methods: Retrospective case series including patients admitted in our comprehensive stroke center for ischemic stroke secondary to carotid web. Demographics, radiological, incidence of recurrent stroke and treatment characteristics were collected.
Results: Three patients were included (66.6% women, mean age 60.3 years). Vascular risk factors were not very frequent: smoking (33%), hyperlipidaemia (33%), diabetes (0%) and hypertension (100%). One patient suffered a transient ischemic attack; the other two patients presented an acute ischemic stroke. Both received intravenous alteplase and mechanical thrombectomy was performed with successful revascularization (TICI 3). In one case, a carotid web was diagnosed after detection in carotid ultrasonography and confirmed by CTA. In the other two patients, it was determined by a CTA performed upon arrival. In two patients dual antiplatelet therapy during three weeks was initiated and in one carotid stenting was performed. After a mean follow up of 11 months (range 25–11) no patients presented new vascular events nor haemorrhagic complications.
Conclusion: In our series both medical and endovascular treatment were safe and no recurrences were detected, nevertheless a longer follow up may be required.
Disclosure: The authors declare no disclosures.

EPO-021

Cerebral edema in acute stroke: effect of thrombolytic treatment

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Background and aims: Cerebral edema (CED) is a life threatening complications of ischemic stroke. Intravenous thrombolysis (IVT) is an effective treatment for acute ischemic stroke but rtPA is thought to activates molecular routes inducing blood-brain barrier disruption and thus increasing the risk of CED and hemorrhagic conversion. The aim of the study is to assess the role of rtPA in CED development, evaluating edema formation and growth in IVT-treated and non-treated patients.
Methods: We selected patients affected by anterior circulation ischemic stroke with a definite CT scans follow-up at 240±12 hours (T1), 72±24 hours (T2) and 120±24 hours(T3) from stroke onset. At each time-points lesion volume was assessed through multiplanar reconstructions along coronal, sagittal and axial planes. To estimate the lesion volume growth, we evaluated the percentage increase of lesion volume and the growth velocity of CED, considered as ratio between volume difference at different points and the difference of time expressed in hours.
Results: We observed a significant increase of ischemic lesion volume between Vol1 and Vol2 in IVT patients compared with n-IVT patients (respectively 68.2% and 50.1; p=0.041). We observed was a significantly higher CED rate between T2 and T1 in treated patients compared with untreated patients (respectively 1.7cm^3/h and 0.87 cm^3/h; p=0.035).
Conclusion: In our study we demonstrated an increase in the growth rate of CED in the first 72 hours after the ischemic event in rtPA treated patients. Acting on rtPA-induced mediators could help prevents CED occurrence and hemorrhagic conversion.
Disclosure: Nothing to disclose.

EPO-022

Diagnostic features in patients with ischemic stroke by the mechanism of paradoxical embolism

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Background and aims: Paradoxical embolism (PE) is one of cause of ischemic stroke (IS), which occurs when there is an anomaly in the heart in the form of a functioning patent foramen ovale (PFO). The purpose of the study is to identify the clinical and morphological features of patients with PE.

Methods: 46 patients from 18 to 59 years old (32 women (69.57%), mean age 36.8±8.7 years) with IS caused by the mechanism of PE examined. With transthoracic echocardiography, all were found to have PFO sizes from 1 to 3mm with a high degree of shunting blood flow (three and four degrees).

Results: In 11 cases (23.91%) PFO was combined with aneurysm, in 7(15.22%)-with atrial septal hypermobility. In ultrasound examination of the veins of the lower extremities and small pelvis, the presence of "fresh" thrombi was recorded in one case(2.17%), in 2(4.34%) occlusive post-thrombotic sclerosis of the lower extremities veins. In 15 patients(32.6%), prothrombotic risk factors were identified: homozygous mutation(n=1), heterozygous for Leiden's factor(n=2), heterozygous for the fibrinogen gene(n=7), increased factor VIII in combination with von Willebrand factor activity(n=4), APS(n=1). Four patients were taking oral contraceptives.

Conclusion: The study showed that the development of IS by the mechanism of PE is characteristic of young patients with prothrombotic risk factors, isolated(PFO with a high degree of shunting blood flow) and associated defects(PFO, aneurysm, myocardial hypermobility) of the interatrial septum. Ultrasound examination of the veins of the lower extremities and small pelvis is not decisive for suspected paradoxical embolism, which is consistent with the literature data.

Disclosure: The authors declare no financial or other conflicts of interest.

EPO-023

Clinical and imagiological findings of patients with cerebral amyloid angiopathy-related inflammation: a case series

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Background and aims: Intracerebral hemorrhages and cognitive impairment are the most frequent presentations of cerebral amyloid angiopathy (CAA). Cerebral amyloid angiopathy-related inflammation (CAA-ri) is one of its rarest manifestations. Our aim was to investigate patients with CAA who meet CAA-ri diagnostic criteria and to characterize them.

Methods: Retrospective study of all CAA patients diagnosed since 2014, identifying those who fulfilled CAA-ri diagnostic criteria. We analyzed demographic data, clinical manifestations, imagiological findings, treatment and disease evolution.

Results: Of the 69 patients with probable CAA, we found seven patients with probable CAA-ri (one from another hospital center), with an average age of 72 (62–78) and 57.1% of the male gender. In 85.7% of the cases, the CAA-ri was the first manifestation of the CAA. Initial manifestations were persistent focal neurological deficits in 33 patients (42.9%), cognitive impairment in two (28.6%), transitory focal neurological deficits in q (14.3%) and isolated headaches in another (14.3%). Six patients showed unilateral imaging abnormalities and the average number of lobar microhemorrhages was 85 (10–258). All of them presented cortical hemosiderosis and involvement of the parietal lobe. Five patients underwent immunosuppressive treatment, with complete imagiological resolution in four patients, partial resolution in one and aggravation in another. One patient had recurrence of hemorrhagic stroke and another had recurrence of CAA-ri. One death was recorded, while the remainder, at the time of the last contact, had an average mRS of 1 (0-3).

Conclusion: Although definitive diagnosis of CAA-ri is made through anatomopathological study, clinical and imagiological findings also establish it, according to recent criteria.

Disclosure: Nothing to disclose.

EPO-024

Cerebral venous thrombosis in Brazil: a case series and literature review

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Background and aims: Cerebral venous thrombosis (CVT) is a rare cerebrovascular disease. Compared to the European spectrum, there have been few studies in the Brazilian population.
Methods: This is a prospective and descriptive study. The aim is to describe a case series of 31 patients diagnosed with CVT by imaging findings between 2015 and 2020 in Sobral-Ceará, Brazil. Also, to present a discussion and literature review on the subject.
Results: There was a predominance of women, with onset in the fourth decade of life, headache as the most common clinical event (96.8%), and oral contraceptive use as the most common risk factor (54.8%). Three patients presented COVID-19 infection. The transverse sinus was the most affected venous sinus (70.1%), and multiple sinus CVT was a frequent finding (64.5%). Death occurred in two patients.
Conclusion: CVT is a rare cerebrovascular disease, though well studied worldwide. However, in Brazil, it is poorly documented: there have been only four Brazilian case series. The presence of headache and seizures should raise the suspicion of CVT. It presents many known risk factors, which affect the Virchow triad.
Computed tomography is commonly the first requested imaging exam. The treatment aims to recanalize the occluded sinuses or veis, treat the prothrombotic state, and prevent a CVT recurrence. The prognosis is usually good. The characteristics of this series are similar to those of Brazilian populations. It should occur a raise and standardization of Brazilian CVT studies. By a continental comparison, South America presents the lowest number of CVT studies, while Europe presents the highest.
Disclosure: The authors report no conflict of interest.

EPO-025

Outcomes of Endovascular treatment for Acute Ischaemic stroke in Mater Dei Hospital, Malta

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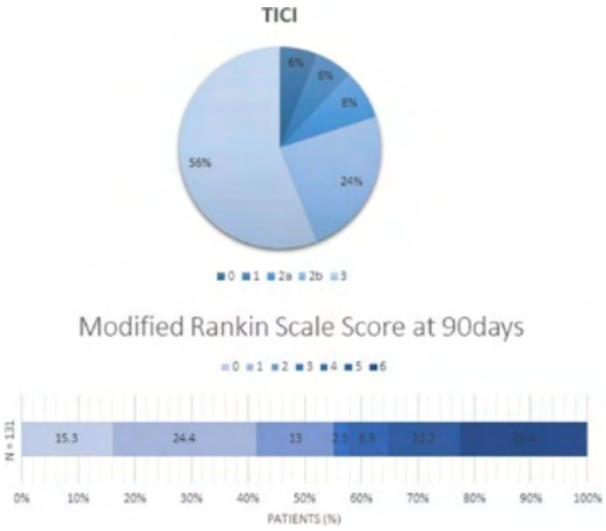
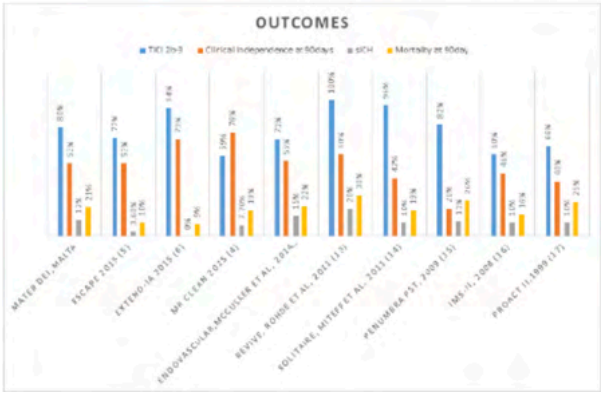
Background and aims: The aim of this study was to assess the outcomes of endovascular treatment for Acute Ischaemic Stroke (AIS) at Mater Dei Hospital, Malta and compare them with international data.
Methods: A prospective review of all patients who underwent mechanical thrombectomy from 2015 till the end of 2019 was performed. Eligible patients had large vessel occlusion confirmed on CT perfusion. Demographical data, NIHSS (The National Institutes of Health Stroke Scale) at presentation, endovascular procedure details and process times were analysed. Thrombolysis in Cerebral Infarction (TICI) score was used to assess the degree of reperfusion. TICI score of 2b–3 was considered as successful recanalization. Functional outcome (modified Rankin Score – mRS) and mortality at 90 days were measured. Functional independence was defined as MRS of ≤2.

Demographics		
	Total no. of patients	131
	Male	63
	Female	68
	Age –yr	
	Mean	71
	Range	25-94
Presentation		
	NIHSS at presentation	
	Mean	14
	Range	2-32
	Affected side- clinically	
	Right	65
	Left	64
	Others	2 – basilar occlusion
	Onset of Symptoms	No. of Patients
	00:00 – 08:00	39
	08:01 – 16:00	48
	16:01 – 23:59	35
	Wake-up	4
	Unknown onset	5
	IV Thrombolysis	
	Yes	69 (52.7%)
	No	62 (47.3%)
	Reasons for no Thrombolysis	
	Onset >4.5hours	5
	On oral anticoagulation	22
	Wakeup/Unknown clear onset	10
	Recent invasive procedure	6
	Recent history of bleeding	1
	Active Malignancy	6
	Head injury	2
	Low NIHSS/rapidly improving	5
	Other medical contraindications	5
Process times		Mean – mins
	Door to CT	35 (range 5-218)
	CT to Puncture	78 (range 11-282)
	Onset to Puncture	199 (range 56mins-18.04hrs)

Results: A total of 132 patients underwent endovascular treatment, one patient was excluded due to incomplete data. The mean age was 71 (range 25–94), and the mean NIHSS at presentation was 14. Of the 131 patients treated, 69 received intravenous thrombolysis. Successful recanalization (TICI 2b–3) was achieved in 80% of patients (105/131). 53% of patients (69/131) achieved Functional independence at 90, with a mortality of 21% at 90 days. Symptomatic intracranial hemorrhage was recorded in 16 patients (12%) There was a statistical difference in the functional independence and mortality rate in favour of the successful recanalization group.



Subgroups	Total- %, (no./total no)	Functional Independence (MRS ≤2) at 90 days - %, (no./total no)	sICH - %, (no./total no)	Mortality at 90days - %, (no./total no)
Successful recanalisation(2b-3)	80.2% (105/131)	81.3% (65/105)	9.5% (10/105)	15.2% (16/105)
Unseccessful recanalisation (0-2a)	19.9% (26/151)	15.4% (4/26)	23.1% (6/26)	46.2% (12/26)
TICI 0/1	12% (16/131)	1.5% (2/131)	1.5% (2/ 131)	6.9% (9/131)
2a	8% (10/131)	1.5% (2/131)	3.1% (4/131)	2.3% (3/131)
2b	24% (32/131)	16.0% (21/131)	1.5% (2/131)	5.3% (7/131)
3	56% (73/131)	33.6% (44/131)	6.1% (8/131)	6.9% (9/131)
Thrombectomy only	47.3% (62/131)	45.2% (28/62)	9.7% (6/62)	29.0% (18/62)
Thombolysis + Thrombectomy	52.7% (69/131)	59.4% (41/69)	14.5% (10/69)	14.5% (10/69)
Overall	131	52.7% (69 out of 131)	12.2% (16 out of 131)	21.4% (28 out of 131)



Results and comparison

Conclusion: Our data is consistent with favourable clinical outcome after successful recanalization. Service at Mater Dei Hospital is achieving favourable outcomes for patients treated with mechanical thrombectomy for AIS.
Disclosure: Nothing to disclose.

EPO-026

Platelets inhibitory effect of rtPA in patients with acute stroke

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Background and aims: Recombinant tissue plasminogen activator (rtPA) is widely used to treat acute ischemic stroke. In vitro studies and in vivo cardiologic studies showed a possible platelet inhibition by rtPA. The aim of our study was to investigate if platelets are inhibited by rtPA also in patients with acute ischemic stroke.

Methods: We performed a retrospective study including consecutive patients with acute ischemic stroke admitted to our Stroke Unit in whom platelet testing was performed within 24 hours from admission. We included patients on antiplatelet therapy before the event and analyzed them separately according to the antiplatelet. We compared platelet inhibition in patients treated and not treated with rtPA. Platelet aggregation was evaluated with electrode impedance aggregometry after stimulation with arachidonic acid (ASPI test) and ADP (ADP test). ASPI test is usually reduced if platelets are inhibited with acetylsalicylic acid. ADP test is usually reduced if platelets are inhibited with P2Y12 inhibitors.

Results: We included 162 patients treated with rtPA and 151 controls. rtPA infusion was associated with lower ADP test among patients on acetylsalicylic acid before admission and a trend for lower ASPI test among patients on P2Y12 inhibitors (see table 1). We did not find significant differences of ADP test or ASPI test in patients on dual antiplatelet therapy.

	Treated with rtPA median (interquartile range)	Controls median (interquartile range)	P value
Patients on acetylsalicylic acid	(n = 114)	(n = 108)	
ADP test	54.0 (35.0 – 70.0)	58.0 (44.3 – 84.8)	**0.02**
ASPI test	20.0 (12.0 – 35.3)	22.0 (16.3 – 41.8)	0.08
Patients on P2Y12 inhibitors	(n = 32)	(n = 26)	
ADP test	30.0 (15.0 – 53.3)	31.5 (18.0 – 46.3)	0.94
ASPI test	58.0 (36.0 – 90.5)	80.5 (46.5 – 102.0)	0.15
Patients on DAPT	(n = 16)	(n = 17)	
ADP test	40.0 (15.0 – 68.0)	37.0 (22.0 – 62.0)	0.87
ASPI test	17.0 (8.3 – 41.8)	18.0 (7.5 – 25.5)	0.58

table 1. Comparison of platelet inhibition between patients treated with TPA and controls according to the antiplatelet agent used before admission

Conclusion: We found a possible rtPA mediated platelet inhibition in patients with acute ischemic stroke, particularly involving ADP pathway. If confirmed, our findings might be relevant for clinical decision making, when early administration of antiplatelets is considered after rtPA.

Disclosure: Nothing to disclose.

EPO-027

Abducens neuropathy in Giant Cell Arteritis: you find what you seek!

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Background and aims: Giant cell arteritis (GCA) is the most common idiopathic systemic vasculitis, affecting large and medium-sized arteries, mainly the branches of arteries originating from the aortic arch. Neurological manifestations are common and varied.

Methods: N/A

Results: A 76-year-old woman with a prior history of migraine without aura presented with new-onset acute horizontal binocular diplopia. Neurological examination revealed left lateral rectus palsy and horizontal binocular diplopia in primary gaze position and, mostly, on left gaze. A more thorough questioning uncovered a history of holocranial headache (mostly frontal, pulsatile, severe, with photo, phono and kinesiophobia, and worsening with Valsalva manoeuvre and during night-time), scalp hypersensitivity, mandibular claudication, myalgia, and weight loss in the previous two months. Blood tests showed normochromic normocytic anaemia, thrombocytosis, and elevation of C-reactive protein, sedimentation rate and ferritin. No acute lesions were present in the brain MRI. Considering the diagnosis of GCA-related abducens neuropathy, corticotherapy was promptly initiated. Ultrasound evaluation of temporal arteries revealed bilateral hypoechoic oedematous wall swelling ("halo sign") and guided biopsy eventually confirmed GCA. Whole-body fluorodeoxyglucose positron emission tomography demonstrated uptake in the vertebral arteries. The patient improved and at discharge maintained just a slight diplopia in relation with mild left lateral rectus palsy, without further symptoms or impairment.

Conclusion: Abducens neuropathy is rare in the context of GCA but should be promptly recognized as part of the spectrum of neurological manifestations of this pathology. A high degree of suspicion is warranted since early diagnosis and treatment are essential to prevent serious sequelae.

Disclosure: Nothing to disclose.

EPO-028

Carotid web: a rather elusive cause of cryptogenic stroke

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Background and aims: Carotid web (CW) is a fibrous shelf-like membrane with intraluminal protrusion, usually arising from the posterior wall of the carotid bulb. It is considered a rare form of focal intimal fibromuscular dysplasia and has been increasingly recognized as a cause of embolic stroke of undetermined source (ESUS). The diagnosis is challenging, often requiring a digital subtraction angiogram (DSA). The optimal treatment approach remains controversial.
Methods: N/A
Results: A 49-year-old female was admitted to the emergency department after experiencing two transient episodes of new-onset aphasia, right facial droop, and right-sided weakness. Complete recovery ensued after five and 20 minutes respectively. Neurological examination on admission was unremarkable. Head CT was normal, while CT angiography showed occlusion of the M2 segment of the left middle cerebral artery (MCA). Recurrence of symptoms (mild aphasia, right central facial palsy and right hemiparesis) was observed three hours after the initial event. As such, intravenous thrombolysis was started, followed by mechanical thrombectomy. DSA found no occlusion, but documented a CW on the left carotid bulb. The patient recovered fully. Brain MRI confirmed an acute ischemic stroke in the MCA territory. Since the remaining investigation was unremarkable, the diagnosis of ischemic stroke secondary to the CW was established, and endovascular stenting was performed. No neurological sequelae or further events were noticed at 3-month follow-up.
Conclusion: This case illustrates the importance of considering CW as a potential cause of ESUS, particularly at a young age. Timely diagnosis and early treatment are essential to reduce the risk of stroke recurrence.
Disclosure: Nothing to disclose.

EPO-029

Cerebral leucoencephalopathy due to TREX1 mutation

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Background and aims: TREX1 gene encodes 3'DNA repair exonuclease-1 and mutations have been associated with autoimmune and cerebroretinal vasculopathy syndromes. Our main objective is to describe a patient with leucoencephalopathy due to TREX1 mutation.
Methods: Single-case report.
Results: A 64-year-old woman, was admitted for having speech impairment and agitation, followed by progressive worsening of the state of consciousness over the course of a day. Her medical background included episodes of bilateral anterior uveitis, polyarthralgias, parapsoriasis and a constitutional syndrome (fever, asthenia, weight loss) since 1–2 years ago. During the last year she had been followed at ambulatory appointments for a tension-type headache. No family history of neurological diseases or consanguinity. At admission, she was awake, inattentive, agitated. She was able to say hello, but unable to name, repeat or accomplish orders, without any other changes in neurological examination. Also, she was apyretic and hemodynamically stable. Cerebral-CT/angioCT were normal. CSF presented 49cells/uL (59%lymphocytes), 1.18g/L proteins. She improved progressively in few days. From the study completed we emphasize: Cerebral-MRI: multiple T2/FLAIR hypersignal areas corresponding to small vessel disease in semioval centers, frontoparietal and anterior temporal lobes, without microhemorrhages or vasculitis at angioMRI. Laboratory findings: mild anemia and thrombocytopenia, C-reactive protein 51mg/L and erythrocyte sedimentation rate 42mm/h. Genetic testing: previously unreported TREX1 mutation (c.347C>A,Pro116Gln). Ophthalmological evaluation showed decreased bilateral visual acuity. Fluorescein-angiography was normal.
Conclusion: We present a rare case of a patient with TREX1 mutation, which diagnosis is challenging due to the symptoms variability.Correctly identifying this entity is important to spare patients from harmful treatments, invasive procedures and genetic counseling.
Disclosure: No disclosures to present.

Child neurology/developmental neurology

EPO-030

Neurological co-morbidities of Turner Syndrome: a systematic review

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Background and aims: Turner Syndrome (TS) is a genetic disorder characterized by partial or complete X monosomy (45X0).Its main clinical features involve ovarian failure, short stature, and increased risk of cardiac and autoimmune abnormalities. Although a wide spectrum of neurological co-morbidities has been described, clinicians have relatively little awareness and there is still no systematic review focusing on the neurological aspects of TS. Our aim was to systematically investigate the relationship between these abnormalities and TS.
Methods: We performed a systematic search on MEDLINE database using as keywords: "Turner syndrome", "neurological", "neurodegenerative", "neurodevelopment", "genetic", "co-morbidities", "autoimmunity" "epilepsy", "cognition" and "cerebrovascular". Clinical studies (case-reports, case-series, clinical trials) published until 01/2021 were included.
Results: Of a total of 538 identified relevant articles, 26 studies were included. Fragile-X, Duchenne/Becker muscular dystrophy, X-linked dystonia-parkinsonism, Neurofibromatosis Type1, mitochondrial disorders, pseudotumor cerebri, Chiari I malformation, meningiomas, glioblastoma multiforme, stroke, cerebrovascular malformations, hearing loss, cognitive impairment and epilepsy were reported to be potentially associated with TS. Cerebrovascular malformations due to congenital hypoplasia could contribute to cerebral infarction. About half TS cases revealed abnormalities on brain MRI, including pachygyria, lissencephaly, and partial agenesis. Most TS cases with epilepsy showed poor response to anti-epileptic drugs. Estrogen replacement did not majorly affect cognitive deficits of adults with TS.
Conclusion: TS may be associated with a wide range of genetic and non-genetic neurological diseases, highlighting the need of increased clinical awareness, the potential impact on treatment decisions, and the possible contribution of X-chromosome genes to neurodevelopmental, cerebrovascular, epileptic, and cognitive disorders. Longitudinal and larger studies are needed to confirm these findings.
Disclosure: Nothing to disclose.

EPO-031

Hypomyelinating leukodystrophy type 9: case report of an extremely rare disorder

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Background and aims: Hypomyelinating disorders of the central nervous system are still a diagnostic challenge, as many patients remain without genetic diagnosis. Variants within RARS gene have been recently associated with hypomyelinating leukodystrophy type 9 (HLD9). We hereby describe the clinical and neuroimaging features of the 1st case of HLD9 in Portugal.
Methods: Clinical Case
Results: We describe a male toddler, born at 40-weeks gestation from an uncomplicated pregnancy and delivery to unrelated parents. He first came to medical attention at the age of 15 months because of motor delay with toe posturing and poor eye fixation. Neurological examination at 18 months revealed strabismus without nystagmus, some dystonic movements and severe spasticity of his legs. Deep tendon reflexes were brisk with ankle clonus and extensor plantar responses bilaterally. He presented a spastic gait and could not stand without assistance. A brain-MRI scan at 18 months showed supratentorial white matter hypomyelination without atrophy of the corpus callosum, cerebrum, or cerebellum. A Next-generation sequencing (NGS) panel revealed compound heterozygous mutations in RARS1 gene: c5A>G(p.(Asp2Gly)) and novel c.370-2A>G(r.spl). Parents' study confirmed the segregation. Currently, aged three, symptomatic management includes botulinum toxin and rehabilitation – he is able to walk with bilateral support. He came to develop an oscillatory nystagmus and a language impairment.
Conclusion: This index patient is the ninth reported case of HLD9 caused by RARS1 gene mutations, which emerges as a key player in myelination. This highlights the importance of symptoms and MRI-pattern recognition and the use of NGS techniques to enlarge molecular diagnosis of hypomyelinating disorders.
Disclosure: Nothing to disclose.

EPO-032

Changes in the neuronal morphology at the hippocampus produced by maternal separation in mice

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Background and aims: In the early stages of developing certain genetic and environmental factors such as social exclusion can influence the maturation of the central nervous system causing changes in neuronal microanatomy, such as the density and morphology of neurons and their dendrites. Maternal separation is a model in which, during the postnatal period, puppies are isolated from their mother, in order to induce stress to the offspring and to study the effects of maternal care and its implications for humans.
Methods: Experimental study. A sample of 18 mice was used; nine controls and nine experimental, the mice were separated for two hours from 7:00–9:00 am, with sensory deprivation of the mother. Mice were sacrificed and brains processed. Histological analysis was performed locating the hippocampus and dividing it into the four main regions (CA1, CA2, CA3, and tooth rotation). An average of each region was obtained and compared with Student's T.
Results: Lower neuronal density was obtained in SM mice in CA1 (2,480), CA2 (1,960) and in CA3 (1,488) in contrast to the control mice in CA1 (3,324), CA2 (3,054) and CA3 (2,395). The morphological analysis of the dendrites resulted in a 31.66% decrease in the dendritic branches of the mice belonging to the maternal separation group with respect to the control group.

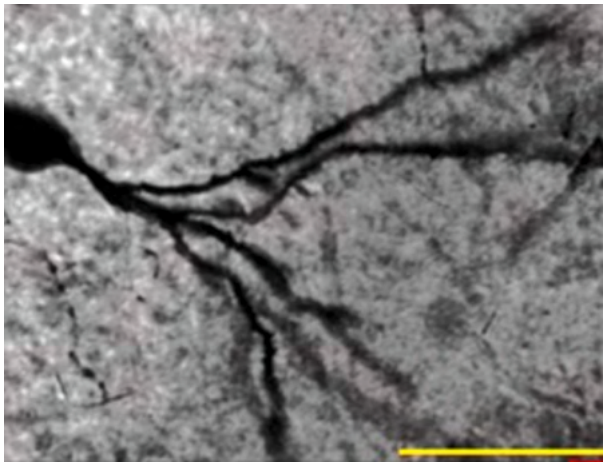

Fig 1. Hippocampal neuron and their branches belonging to the control group.

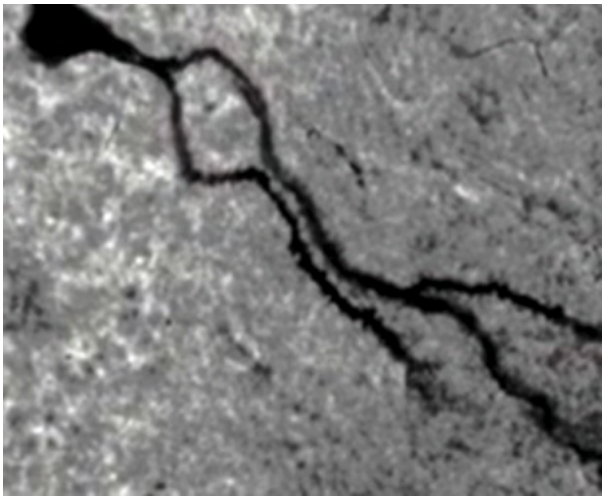

Fig 2. Hippocampal neuron and their branches belonging to the maternal separation group.

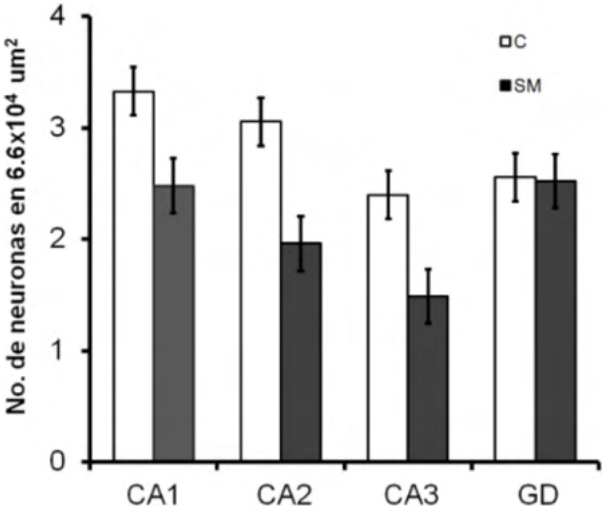

Fig 3. The image shows the mean number of hippocampal neurons by area.

Conclusion: Stressful experiences, such as maternal separation, at an early age cause changes at the hippocampus level, such as alteration in cell number and in the morphology of dendrites and their spines.
Disclosure: The author have no financial conflicts of interest to disclose concerning the presentation.

EPO-033

Refractory status epilepticus in children

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Background and aims: The aim of this research was evaluation of clinical and etiological profile of refractory status epilepticus (RSE) among children aged between one month and 18 years.
Methods: The study was done between January 1, 2017 and December 24, 2019. All children with the age limits mentioned above, who presented convulsive epileptic status (SE), subsequently with development in RSE (refractory status epileptic), were included in the study. Patients were investigated and evaluated according to a standard protocol. Subsequently, the characteristics of children with RSE and those without an evolution in RSE were compared.
Results: 55 children, out of whom 32 boys with SE were enrolled in the study, of which 20 children (36%) developed RSE. CNS infections were the most common causes in SE and development of RSE (51% in SE and 53% in RSE, $p>0.05$). Noncompliance of antiepileptic medication served as the second cause for evolution in RSE. The overall mortality rate was 10.9%, the chances of death in RSE (20%) being higher than in SE (5.7%). The unfavorable prognosis was seven times higher in children with RSE, compared to children who developed SE (PR=7.0; 95% CI:1.6–22.3).
Conclusion: In the management of CNS infections, pediatricians should be aware of the high risk of developing RSE. In addition, the possibility of developing RSE should be considered and promptly managed in an intensive care unit in order to reduce the risk of mortality and morbidity of this severe neurological condition.
Disclosure: Nothing to disclose.

EPO-034

Neuropsychomotor development in normocephalic children exposed to Zika Virus: a literature review

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Background and aims: Zika Virus infection, evident in 2015 and 2016 in the Northeast region of Brazil, was responsible for affecting the Central Nervous System and, mainly, the neuropsychomotor development of newborns. Being able to be born with microcephaly or normocephalic, moderate or severe neurological abnormalities such as hearing loss, visual impairment and arthrogryposis may be present, directly compromising the babies's quality of life.
Methods: This work is a literature review, in which scientific articles were searched in the PUBMED database and the VHL Regional Portal, in which only articles in English with primary data were considered, without year restriction, having as the following research formula results: "((development) AND (normocephalic children)) AND (Zika Virus)".
Results: The search resulted in six articles, of which five were selected according to the exclusion criteria. The five studies found were cohorts, which indicate that normocephalic children who were exposed to ZV in the intrauterine period may suffer from developmental delays. Three of the studies worked with children up to 18 months of age while the other two ranged from six to 40 months. The scales used were different in each study. However, everyone realized that these children may suffer from delayed language, cognitive and motor development.
Conclusion: The literature reports that children who had contact with ZV in the prenatal period and were born normocephalic suffer from other influences of the virus, and may suffer delays in development and therefore need more detailed monitoring. However, more longitudinal, multicenter studies are needed to assess the development of these children
Disclosure: Nothing to disclose.

EPO-035

Long term disability progression in early and late onset pediatric multiple sclerosis patients

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Background and aims: Previous studies identified different clinical and MRI features in early and late onset pediatric multiple sclerosis (LOPMS) patients. The aim of this study is to evaluate long-term disability progression in EOPMS and compare to LOPMS.

Methods: A retrospective cohort study using prospectively collected clinical information from the Italian MS Registry was analyzed. Cox proportional hazards regression models adjusted for sex and disease modifying treatment (DMT) exposure were used to assess the risk of reaching sustained Expanded Disability Status Scale (EDSS) 3, 4, and 6 in EOPMS (MS onset ≤11 years) and LOPMS (MS onset >11 years).

Results: A total of 1,170 PMS patients were included; 174 (15%) were classified as EOPMS. A greater proportion of males was observed in EOPMS compared to LOPMS cohort (43% vs 30%; $p<0.001$). Compared to LOPMS cohort, the EOPMS cohort took longer to reach all three disability milestones from their MS onset (sustained EDSS 3: hazard ratio [HR] 0.58; 95% confidence interval [CI] 0.43–0.79; sustained EDSS 4: HR: 0.44; 95% CI: 0.30–0.63; sustained EDSS 6: HR 0.44; 95% CI 0.28–0.72; $p<0.001$), independently from DMT exposure. EOPMS and LOPMS reached all three disability milestones at the same ages.

Conclusion: The longer time took to reach the main disability milestones observed in EOPMS compared to LOPMS cohort underscore a greater capability to counteract brain damage in younger patients that is likely to decrease with aging. Moreover, these findings suggest the existence of pathophysiological mechanisms specific for MS patients with very early onset.

Disclosure: Nothing to disclose.

EPO-036

Glutaric aciduria type I: Study of a tunisian cohort

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Background and aims: Glutaric aciduria type1(GA1) is a rare autosomal recessive disorder caused by a defect of the glutaryl-CoA dehydrogenase. Diagnosis can be difficult due to clinical and evolutionary variability. We aimed to present the clinical and paraclinical characteristics of a Tunisian cohort of children with GA1.

Methods: We conducted a retrospective study in the Department of Child and Adolescent Neurology of the National Institute Mongi Ben Hmida of Neurology of Tunis between 2005 and 2019, including patients with GA1. Clinical and paraclinical data were analysed.

Results: 15 patients were included: six males and nine females. Mean age at onset was 11 months. 2/3 of patients came from a consanguineous marriage and four patients had a family history of AG1. Two patients were asymptomatic, 10 had a psychomotor delay and three a psychomotor regression “encephalitis-like”. Main Neurological features were dystonia (73 %), spasticity(5/15) and macrocephaly(4/15). All patients had preserved intellect. Brain MRI showed T2 hyperintensities in basal ganglia (10/15), dilated sylvian fissures (9/15), and subdural collections (2/15). AG1 was confirmed by chromatography of organic acids (12/15) and genetic study (3/15). Five patients received carnitine supplementation and eight patients a diet restricted in Lysine and Tryptophan. No further decompensations were observed and dystonia worsened in most cases.

Conclusion: Our study highlights the phenotypic heterogeneity of GA1 ranging from asymptomatic cases to early encephalitic-like syndrome. MRI is helpful for the diagnosis which is easily done by urine testing for organic acids. Early and appropriate treatment can improve prognosis and allow genetic counseling.

Disclosure: No disclosures

EPO-037

Children with congenital heart disease have specific impairments in neurocognitive functions

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Background and aims: Children with congenital heart disease (CHD) have a risk for neurodevelopmental disorders. However, we need to do further research for revealing the specific effects of CHD on development of neurocognitive functions. The aim of this study was to further address the neurodevelopmental consequences of CHD across different neurocognitive functions in preschool children by using complex child neuropsychological assessment.
Methods: The experimental group included 14 preschool children at the age of 5–6 with diagnoses of Class 1 CHD, with no genetic or chromosomal abnormalities. The control group included 14 typically developing children. Children from experimental and control group were matched for gender and age. Children from both groups were assessed with Luria's neuropsychological assessment battery which consists of 16 subtests for assessing visuospatial functions, memory, sensorimotor functions, language and executive abilities.
Results: One-way ANOVAs by group revealed significant differences (p=0,05) between groups for performance of neuropsychological subtests which designed to asses executive functions (reaction of choice, visual attention, following instructions) and sensorimotor functions (imitating hand positions, manual motor sequences and drawing the fence). Children with CHD performed these subtests significantly worse.
Conclusion: In view of the obtained results it can be assumed that CHD can cause the delay in the development of executive and sensorimotor functions in children at the age of 5–6. We have revealed that CHD have specific (not global) negative effect on development of neurocognitive functions in children. However, it necessary to do further researcher for revealing the influence of CHD on neurocognitive development of children.
Disclosure: Nothing to disclose.

EPO-038

Prevalence of Mental Development Delay and Intellectual Impairment Among Survivors of Perinatal Arterial Ischemic Stroke

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Background and aims: Perinatal arterial ischemic stroke (PAIS) defines the focal disruption of cerebral blood flow between 20 weeks of gestation and postnatal day 28. Possible motor results of this event are well established in literature, but the full spectrum of developmental outcomes remains controversial. This study aims to evaluate the rates of mental development and intellectual impairments following PAIS.
Methods: A systematic review of the literature was performed according to PRISMA's guidelines. The search formula applied to PubMed, WebOfScience and LILACS was: ((((“cognitive”) OR “neurodevelopmental”) OR “mental performance”) AND (“neonatal” OR “perinatal”)) AND “stroke”. We only included observational studies accessing either Bayley Scales of Infant Development's Mental Development Index, 2nd edition (BSID-MDI-II), or full-scale intellectual quotient (FSIQ) through age-appropriate Weschler Intelligence Scales. Data of patients with perinatal stroke other than PAIS and/or prematurely born were excluded.
Results: Of 255 articles found, 54 were selected for full-text reading, of which 12 were incorporated in our synthesis – seven addressing BSID-MDI-II (total number of patients: 203; age range: 1–3.7 years old) and five focusing on FSIQ scores (total number of patients: 127; age range: 4.3–12.4 years old). When accessed with BSID-MDI-II, 22% of PAIS survivors presented with mental delay (score <70). Among the FSIQ-evaluated, 11% had extremely low intellectual ability (score <70).
Conclusion: This analysis suggests a moderate proportion of negative mental development outcomes amidst PAIS's patients. A possible reason for perinatal stroke not being enormously decisive for future cognitive abilities is babies' elevated neuroplasticity. Still, due to studies' discrepancies, longitudinal-multicentric approaches remain necessary.
Disclosure: This study is not receiving funding from any commercial organizations. All authors declare that neither this study nor one with substantially similar content has been submitted, accepted or published elsewhere.

EPO-039

Prevalence and localization of recurrent backbone pain in adolescents with Internet addiction

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Background and aims: Internet addiction (IA) is a relatively new psychological phenomenon, most commonly marked in socially vulnerable groups (e.g., in adolescents and young adults). Numerous studies have convincingly demonstrated IA comorbidity with a broad range of psychopathologic conditions such as depression, anxiety, and hyperactivity. Recurrent headache and backbone pain are common comorbidities in adolescents with psychological problems. Data regarding backbone pain prevalence and localizations in IA adolescents, however, are limited.
Methods: 4,766 urban Siberian (Krasnoyarsk, Abakan, Kyzyl) school-based adolescents (aged 12–18) were tested with Chen Internet Addiction Scale (CIAS). Based on the CIAS, score Internet users were categorized into three groups: adaptive Internet users (AIU, scoring 27–42, n=2,479); maladaptive Internet users (MIU, scoring 43–64, n=1,951), and pathological Internet users (PIU, scoring 65, 336). Recurrent backbone pain was defined as follows: pain frequency >2 in the month AND typical pain severity three points on the 5-point visual pain scale. 2-tailed chi-square and Kruskal–Wallis tests were used.
Results: Significant positive associations were detected between CIAS scores and recurrent backbone pain prevalence (AIU – 7.1 %, MIU – 11.4 %, PIU – 22.6 %, p<0.001). We didn't find any association between backbone pain typical localizations and CIAS score (Fig. 1, Kruskal–Wallis test p=0.582).

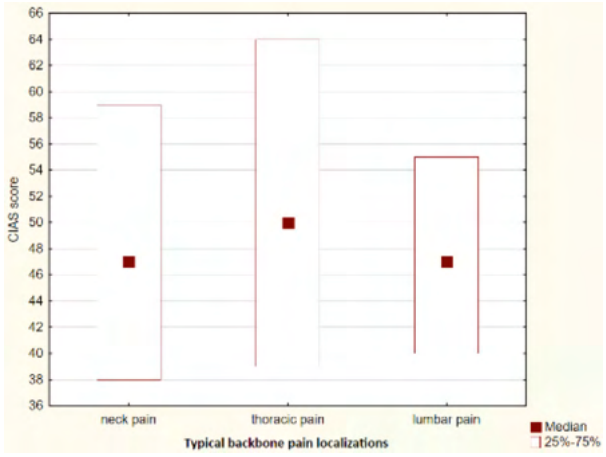

Figure 1. CIAS scores in different backbone pain typical localizations in Siberian adolescents.

Conclusion: Internet-addicted adolescents have significantly higher recurrent backbone pain prevalence that may be explained by the presence of common risk factors such as emotional stress, depression, and anxiety.
Disclosure: We have nothing to disclose.

EPO-040

Association between HLA gene polymorphism and cutaneous adverse reactions caused by antiepileptic drugs

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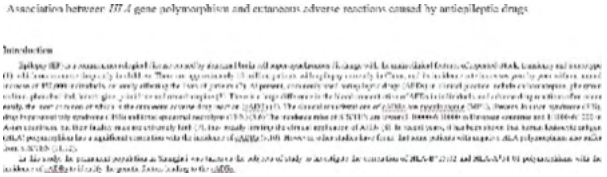
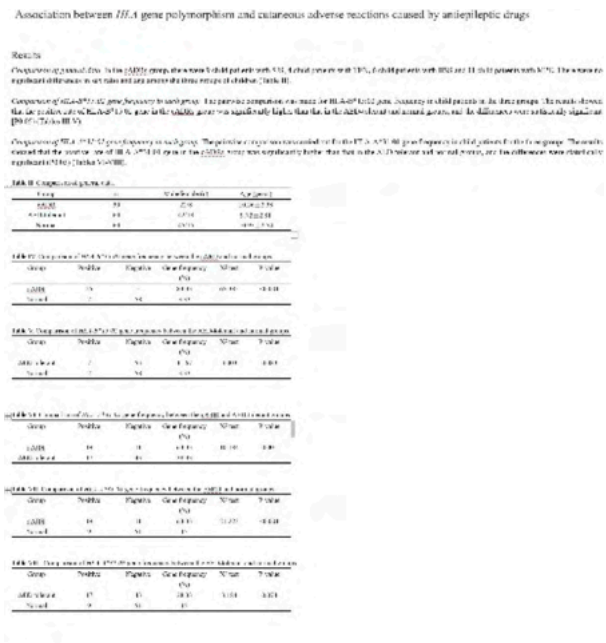
Background and aims: There are approximately 10 million patients with epilepsy currently in China, seriously affecting the lives of patients. Adverse drug reactions of antiepileptic drugs often occur easily, the most common of which is the cutaneous adverse drug reaction (cADR). In recent years, it has been shown that human leukocyte antigen (HLA) polymorphism has a significant correlation with the incidence of cADRs.



Methods: Through the case-control study, 30 child patients with AED-induced cADRs (cADRs group), 60 AED-tolerant child patients (AED-tolerant group) and 60 normal children not taking AEDs (normal group) were collected. The HLA-B*15:02 and HLA-A*31:01 genotypes were detected using the polymerase chain reaction-sequence-specific oligonucleotide (PCR-SSO) probe method, and the correlation of HL A-B*15: 02 and HL A-A*31: 01 genes with the incidence of cADRs was analyzed.

Results: The positive rate of HL A-B*15: 02 gene was 83.33% in the cADRs group, which was significantly increased compared with that in the AED-tolerant and normal groups ($p<0.01$). The positive rate of HL A-A*31: 01 gene was 63.33% in the cADRs group, which was obviously increased compared with that in the AED-tolerant and normal groups $p<0.01$). There were no significant differences in HLA-B*15:02 and HLA-A*31:01 genotypes between the AED-tolerant and normal groups ($p>0.05$).


Association between *HLA* gene polymorphism and cutaneous adverse reactions caused by antiepileptic drugs

Results

Results

Conclusion: The results showed that HLA-B*15:02 and HLA-A*31:01 are significantly associated with cADRs in a Chinese Han population in Shanghai, suggesting that HLA-B*15:02 and HLA-A*31:01 genotypes should be detected in the application of AEDs.
Disclosure: The authors declare that they have no competing interests.

EPO-041

Cerebral folate deficiency: case report of a potentially disabling but also treatable neuropsychiatric disorder

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Background and aims: Cerebral folate deficiency (CFD) is a neuropsychiatric disorder characterized by low levels of cerebrospinal fluid (CSF) 5-methyl-tetrahydrofolate (5-MTHF) but normal systemic folate metabolism demonstrating a decreased uptake of folate into the CNS due to impaired folate receptor function.
Methods: We report a case of CFD.
Results: A girl with normal development presented with ataxia and loss of motor skills at nine months of age. At one year of age the patient developed focal seizures and at two years of age presented with generalized seizures, psychomotor delay, unrest, irritability and stereotyped behaviours. EEG showed right temporal epileptic activity. Brain MRI showed bilateral frontal hypomyelination, patchy frontoparietal and basal ganglia calcifications and cerebellar atrophy. Laboratory blood tests revealed the total folate was 5.2 nmol/L (reference 5.7-31.3 nmol/L) and CSF 5-MTHF was 7nmol/L (reference 35-124 nmol/L). Whole exome sequencing revealed a folate receptor alpha (FOLR1) homozygous c.330_333 duplication. The patient was started on oral calcium folinate, but due to poor response was switched to intravenous administration, after which there was a reduction in seizure frequency.
Conclusion: The clinical picture, laboratory evaluation and exome sequencing revealed the underlying etiology of the detected CFD. Since CFD can be managed with calcium folinate, it is important to identify patients with this condition as early as possible so that they can better benefit from treatment. Recommendations regarding the use of oral or intravenous calcium folinate are not yet available, thus it is important to collect the experience of different centres.
Disclosure: The authors report no conflict of interest.

EPO-042

Abstract Withdrawn

COVID-19 1

EPO-043

Systematic Review of Case Reports: Different types of Encephalitis in SARS-Cov-19 infection reported in 2020

Z. Abbas [1], Z. Sardar [2]
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[2] *Karachi, Pakistan*

Background and aims: Neurological involvement is associated with a severe type of coronavirus disease. The purpose of this study was to delineate the different types of encephalitis reported in COVID-19 disease. The other objective was to summarise the clinical presentation, imaging findings, treatment and outcome of encephalitis in the coronavirus disease 2019 by reviewing case reports.
Methods: We reviewed medical databases PubMed, Google Scholar, Scopus, and MedXriv without any restriction using keywords "Encephalitis", "ADEM", "Haemorrhagic encephalitis" and "necrotising" encephalitis in SARS-Cov-19. We screened and extracted data for demographics, type of encephalitis, clinical features, imaging findings, cerebrospinal fluid findings, treatments and outcomes.
Results: A total of 18 cases included in this systematic review. The mean age was 46.7±16.3. The preponderance of females was observed (55%). ADEM was the predominant type of encephalitis (63.2%). The most common symptom observed was confusion (72.2%). The mean of protein levels in the CSF sample was 128mg/dl. In correlation analysis, positive correlation (r = 0.12) was observed between severity of COVID-19 and outcome calculated by Pearson's correlation coefficient.
Conclusion: Every patient with severe COVID-19 disease presenting with confusion should be screened for possible encephalitis and ADEM. Prompt recognition and appropriate treatment can lower the mortality and morbidity associated with it.
Disclosure: Dr Zaira Abbas and Dr Zomer Sardar have no conflicts of interest or financial ties to disclose.

EPO-044

Systematic Review of Cerebral Venous Sinus Thrombosis in SARS-Cov 19

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[2] *Karachi, Pakistan*

Background and aims: Venous stroke is an infrequent complication of SARS-Cov 19 disease. The main aim of this study is to review the clinical course, radiological manifestations, treatment and outcome associated with venous stroke in covid-19 disease.
Methods: We searched three databases (PubMed, Google Scholar, and Scopus) for published case reports and case series (January 2020 to December 2020). Studies with data of demographics, radiological features, comorbidities, treatments and outcomes were included only.
Results: The average age of the patients was 46±21 years. 61% were males. The most common symptom reported was headache (42.4%) while, less common symptom observed was coma (9.1%). Non-contrast CT/CTV was the investigation of choice in 69% of studies and MRI/MRV was done in 94%. 82% patients were given anticoagulant therapy; treatment was supportive in 6.1%, and 6.1% (2/33) underwent venous mechanical thrombectomy. Mortality occurred at 39%. Positive correlation (r=0.22) was observed between severity of covid and mortality using Pearson correlation coefficient.
Conclusion: Cerebral Venous thrombosis is common in patients with severe COVID-19 disease and co-morbidities. Clinicians should maintain a high index of suspicion for CVT to aid in timely diagnosis and prompt treatment to save lives.
Disclosure: Dr Zaira Abbas and Dr Zomer Sardar have no conflict of interest and nothing to disclose.

EPO-045

Developing a drug-device combination for patients with Parkinson's disease during the COVID19 pandemic

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Rehovot, Israel

Background and aims: ND0612 is a continuous, subcutaneous levodopa/carbidopa delivery system in development for people with Parkinson's disease (PwP). Trials of drug-device combinations typically require several hours of in-person trainings, face-to-face support and monitoring. The conduct of two ongoing international trials had the potential to be impacted by the COVID19 pandemic. We describe the challenges of conducting pivotal studies under the extraordinary conditions imposed by the pandemic.
Methods: A COVID19-Taskforce was established to rapidly adapt study execution strategies and tactics, balancing patient safety with good study practice.
Results: A risk assessment was immediately performed leading to a temporary protocol addendum; almost 70% of onsite study-visits were given the option to be conducted virtually (with clear guidance); the rest (including screening) were required to continue in-person. Local tactics were developed to address the difficulties in conducting virtual visits in countries with limited network infrastructures/ smartphone availability.
Nurse-educator support visits at patient homes were partially replaced by virtual visits, and the nurse call-centre was extended to provide 24/7 patient support. Increased sponsor involvement, such as webinars and increased investigator support, improved communications. Study supplies, including investigational product, were sent directly to patient's homes. COVID19 testing was available for study monitors.
Conclusion: The changes implemented were well-accepted by the investigators and patients and ensured patient safety while maintaining the clinical trial integrity. We found that clear and frequent communication, with a balanced 'hybrid' mix of virtual and in-person approaches, successfully enabled the safe continuation of pivotal clinical trials with this drug-device combination in patients with PD.
Disclosure: Funded by NeuroDerm

EPO-046

Perceived stress level for clinical esidents before and during covid pandemics

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[2] *United States*

Background and aims: COVID pandemic put substantial stress on the medical personnel and other health care practitioners. A life of a medical resident has been difficult even before the pandemics. In this study we discuss whether "COVID era" made substantial changes to the perceived stress level of medical residents in a Russian city
Methods: The Russian version of the 10-question questionnaire for perceived stress was recently validated [V. A. Ababkov et. al, doi: 10.21638/11701/spbu16.2016.202]. In this study we compare the results for two cohorts of medical residents Bashkir Medical University (Ufa, Russia). The data for the first cohort, n=98 were collected in 2019, and the data for the second cohort, n=99, were collected in 2020. The average age in both cohorts was 25 years.
Results: There was no difference in the results before and during the epidemics. The overexertion level was 18.5(0.9) before pandemics and 18.5(0.9) during it, reaction level was 10.4(0.5) before and during pandemic, and the resulting stress was 28.8(1.2) in both cases (the number in parenthesis indicate the error estimate). The stress level was, owever, slightly higher than for the general population before pandemics, mostly due to an overexertion: the levels are 13.62(2.75), 10.82(4.29) and 24.44(6.58) correspondingly.
Conclusion: The perceived stress level of medical residents was higher than in the general population before the pandemics. Surprisingly, it did not increase during the pandemic.
Disclosure: Nothing to disclose.

EPO-047

A Case of Guillain-Barre Syndrome in the Setting of COVID-19

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[1] *Phoenix, United States,* [2] *Clearwater, United States*

Background and aims: Guillain-Barre syndrome (GBS) is an immune mediated polyneuropathy that can present in the acute and chronic setting. Symptoms range from an ascending symmetric numbness and weakness to complete paralysis. This case aims to highlight an uncommon complication of COVID-19. A 49-year-old gentleman with a history of hypertension and hyperlipidemia was hospitalized with a 1-month history of abdominal cramping and diarrhea in October 2020. He was diagnosed with COVID-19 at this time although he did not have any respiratory symptoms. Over the following weeks, he began to notice progressive numbness and tingling in his arms and legs, which was followed by weakness.
Methods: On exam, the patient had full strength in all extremities. He had decreased pinprick below the knees and his biceps, brachioradialis, and Achilles reflexes were absent bilaterally. He was unable to walk on his toes, heels, or in tandem gait.
Results: He underwent a lumbar puncture which showed a protein level of 125 with normal cell counts. Magnetic resonance imaging of the brain, cervical, and lumbar spine were unremarkable. Electromyography and nerve conduction studies were deferred as it would not change the patient's management. The patient completed a 5-day course of intravenous immunoglobulin and his weakness began to improve.
Conclusion: The patient's history, physical exam, and lumbar puncture were consistent with GBS. This syndrome can present after infections including viruses like COVID-19. Most GBS presents as an acute, monophasic illness which the patient appeared to have. Symptoms are usually progressive over a couple weeks and then begin to improve.
Disclosure: Nothing to disclose.

EPO-048

Observations of negative impact of COVID-19 on Parkinson's disease.

V. Chyzhyk [1], A. Boika [1], V. Ponomarev [1], M. Sialitski [2], V. Bahamaz [1]
[1] *Department of Neurology & Neurosurgery, Minsk, Belarus,* [2] *2nd Department of Neurology, Minsk, Belarus*

Background and aims: SARS-CoV-2 is responsible for COVID-19 pandemia and has the ability to neuroinvasion. It is unknown how patients with Parkinson's disease (PD) respond to a COVID-19 infection.
Methods: We have done database analysis to determine the possible impact of the undergone COVID-19 on the course of PD.
Results: Our database contains 138 people with PD. We have identified cases of worsening in the condition of patients with PD after a COVID-19 infection. One patient noted increased stiffness in both hands. After a detailed examination, rheumatoid arthritis (RA) was diagnosed, which wasn't observed before this infection. During the RA treatment, the patient noted an improvement and a decrease of stiffness. We also identified two patients, both females, which developed motor symptoms of PD after COVID-19. In 1–3 months after the infection, they started to notice unilateral stiffness and pain. During the detailed examination, we found an increased muscle tone, according to extrapyramidal type, in one hand, general bradykinesia and hypomimia. One patient had also unilateral rest tremor. In these cases COVID-19 infection was confirmed by PCR, and also bilateral polysegmental pneumonia was detected by CT of the chest organs.
Conclusion: SARS-CoV-2 is followed by anosmia, ageusia, lung and/or gastrointestinal damage. According to the theories of "Hit and Run " infectious agents, entering the central nervous system through the neurons, start the process of neuroinflammation and neurodegeneration, after which they leave the body, however, the process of neurodegeneration continues to develop [1, 2]. Therefore, there is a possibility that the neurological consequences of COVID-19 infection.
Disclosure: Nothing to disclose.

EPO-049

Case Report: Myasthenia Gravis Crisis precipitated by COVID-19 infection

S. Azzopardi [1], K. Cilia [2], J. Pearson [2], N. Vella [3]
[1] Department of Neuroscience, Msida, Malta, [2] Department of Medicine, Mater Dei Hospital Malta, Msida, Malta, [3] Department of Neuroscience, Mater Dei Hospital Malta, Msida, Malta

Background and aims: Covid-19 infection has been linked with multiple neurological complications. Myasthenia Gravis (MG) patients in particular are potentially at greater risk of contracting COVID-19 due to immunosuppression therapy. Prognosis may also be worsened by underlying respiratory muscle weakness. No guidelines currently exist regarding management of COVID-19 patients during a myasthenic crisis.
Methods: N/A
Results: We present a case of MG crisis precipitated by COVID-19 infection in a 67-year old male. The patient was diagnosed in 2003; with thymectomy performed in 2004. He had been stable on Azathioprine and Pyridostigmine for several years. He presented to the Emergency Department due to progressive dyspnoea and fatigue. He also complained of chest pain, chills and a bitter taste leading to reduced oral intake. COVID-19 was diagnosed with PCR testing on the 3rd swab; the initial two swabs having failed to detect the virus. He deteriorated within 12 hours of admission; requiring ITU admission and intubation. Repeat CXR 15 hours after admission showed changes suggestive of COVID pneumonitis. He was treated with intravenous immunoglobulin (IVIG) and Methylprednisolone followed by an oral steroid taper. Azathioprine was temporarily stopped due to sepsis-induced pancytopenia, which responded to G-CSF. He was discharged to a rehabilitation facility after 48 days.
Conclusion: MG crisis in previously controlled patients with no other obvious triggers should raise the alarm for possible COVID-19 infection. Repeated testing may be indicated in select cases. Steroids, IVIG and PLEX are all reasonable treatment options. The increased risk of thrombosis with IVIG should be kept into account.
Disclosure: Nothing to disclose.

EPO-050

The emerging landscape of neuroinflammatory manifestations in patients with SARS-CoV-2 infection

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[1] Department of Neurology, Neurosurgery and Medical Genetics, Chisinau, Moldova, [2] Chisinau, Moldova, [3] Department of Neurology & Neurosurgery, Chisinau, Moldova, [4] Department of Neurology, Chisinau, Moldova

Background and aims: Neurological complications of coronavirus disease-2019 (COVID-19) are being increasingly reported. Here, we present two cases of COVID-19 para-infectious complications involving the central nervous system, namely acute necrotizing encephalopathy (ANE) and longitudinally extensive transverse myelitis (LETM).
Methods: Patients underwent comprehensive diagnostic work-up to rule out other causes of ANE and LETM: blood and cerebrospinal fluid (CSF) inflammatory markers, PCR for SARS-CoV-2/EBV/HSV1,2,6/CMV, anti-MOG and anti-aquaporin-4 antibodies, brain and spinal cord MRI.
Results: 1st case features a 44-years-old man admitted to ICU with altered mental status, bulbar palsy, and bilateral limb ataxia. The naso-/oropharyngeal swabs were positive for SARS-CoV-2 infection. CSF analysis was unremarkable, without detectable SARS-CoV-2 RNA. Brain MRI was characterized by widespread cerebellar and thalamic lesions with a hyperintense signal on FLAIR and DWI, and hemorrhages on SWI. Clinical, CSF and imaging findings were indicative of an ANE. The patient received pulse steroid therapy with a good outcome at discharge. Second case illustrates a 35-years-old breastfeeding woman with confirmed SARS-CoV-2 infection, presenting with upper and lower limb weakness, decreased sensation below the Th8 level, and urinary retention. CSF was dominated by mononuclear pleocytosis, with no traces of SARS-CoV-2 RNA. MRI scan revealed a hyperintense signal on T2 and STIR along the whole thoracic spine. These findings were suggestive of LETM, likely to COVID-19. She received pulse steroid therapy with a gradual improvement of neurological deficits.
Conclusion: Neuroinflammatory syndromes might accompany the course of COVID-19. Cytokine storm triggered by the SARS-CoV-2 infection is thought to account for the emergence of ANE and LETM.
Disclosure: Nothing to disclose.

EPO-051

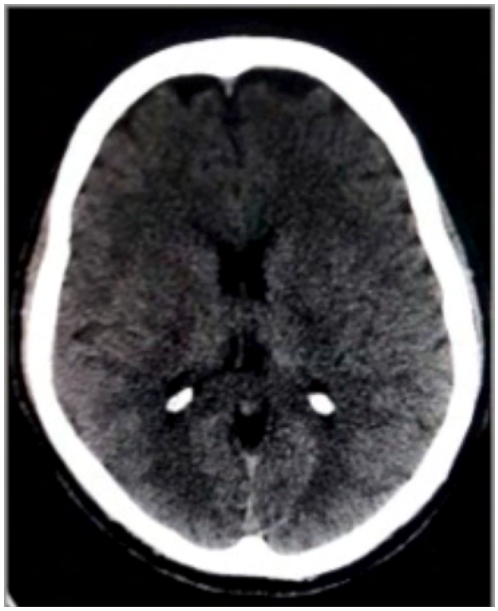
Ischemic stroke associated with COVID-19 in a young patient: a case report

M.F.C. Alves [1], G. Rocha [1], G. Silva [2], A. Da Silva César [3], W. Botelho [4], M. Pereira [4], C. Reis [1], E. Viegas segundo [5], I. Paiva [6]

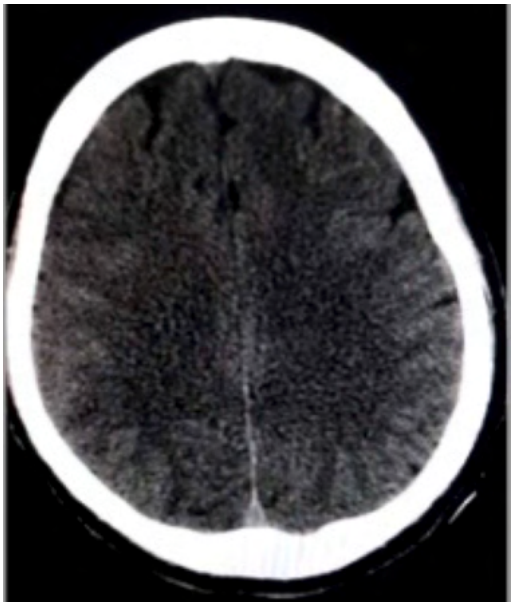
[1] Belo Horizonte, Brazil, [2] Barretos, Brazil, [3] Departamento de Ciências da Saúde, Lavras, Brazil, [4] Lavras, Brazil, [5] Neurologia/neurosurgery, Lavras, Brazil, [6] Emergency room, Três Corações, Brazil

Background and aims: Although it primarily damages the respiratory system, COVID-19 can also develops with neurological conditions such as stroke. This study aims to describe a case report of a patient with ischemic stroke related to COVID-19.

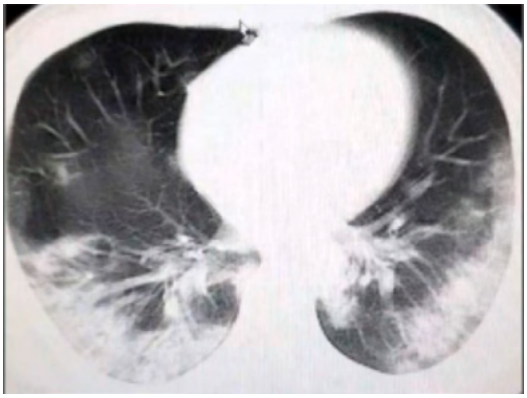
Methods: Male, 44 years old, with untreated diabetes, admitted to emergency with left hemiplegia and dysarthria. Patient had flu-like symptoms 11 days ago and was diagnosed with COVID-19. Auscultation revealed bilateral bases rhonchi. Normotensive, oxygen saturation: 94%, glycemia: 241mg/dl, increased lactate and CRP; hemogram, D-Dimer and coagulogram unchanged. Brain CT demonstrated no evidence of hemorrhagic injury. Chest CT revealed bilateral lung involvement with ground-glass opacities. The patient remained hospitalized for 21 days and was discharged still with motor deficits.



Brain CT evidencing absence of hemorrhagic brain lesions



Brain CT evidencing absence of hemorrhagic brain lesions



Chest CT- 25% involvement of the lung in ground-glass pattern, bilaterally, with predominance in bases and peripheries.

Results: The literature suggests that the mechanisms of ischemic stroke associated with COVID-19 are multiple, highlighting the cytokine storm and coagulation dysfunction. Increased lactate and CRP suggest an acute inflammatory activity; however, the patient did not exhibit high levels of D-dimer, platelet or coagulogram changes. Strokes associated with COVID-19 occur mainly in elderly patients and critically sick. Patients with mild clinical presentation of the disease have an incidence of strokes less than 1%. Although the patient does not have the risk factors mentioned above, diabetes may represent a predisposing factor of the neurological complication.

Conclusion: Patients with mild respiratory conditions may present severe neurological complications, possibly due to the association between previous comorbidity and coagulopathy from COVID-19. The strokes associated with COVID-19 may present greater mortality and disability when compared to cases unrelated to COVID-19.

Disclosure: Nothing to disclose.

EPO-052

The temporality of Anosmia in Patients with COVID19: A Systematic Review

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[1] Salvador, Brazil, [2] Lauro de Freitas – BA, Brazil

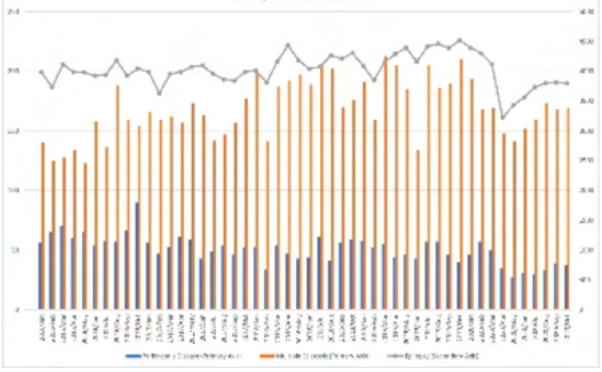
Background and aims: Studies executed during the pandemic on the new coronavirus (COVID-19) demonstrated that complete loss of smell emerged as an important new symptom, however, a qualitative interpretation of this clinical repercussion is still unclear. Thus, it becomes necessary to assess the temporality of anosmia in patients with diagnosis of COVID-19, investigating items such as the period of appearance, duration and recovery rate.
Methods: This systematic review was based on the PRISMA Guideline. The bibliographic search was performed in the PubMed/Medline and Scopus databases using the formula: (Anosmia) AND ((SARS-CoV-2) OR (COVID-19)). Studies with finalized publication, in English, Portuguese and Spanish, addressing qualitative characteristics of anosmia, such as the period of appearance, duration, and persistence rate, in patients diagnosed with COVID-19 were included.
Results: Of 478 articles found, 91 were obtained for full reading, and 21 were included after evaluation by two independent reviewers. In most studies, anosmia manifested after the 3rd day of illness. For patients whose recovery occurred, the duration of the symptom varied from five to 30 days after the condition onset, limited to eight days in 42,8% of articles, with a persistence rate between 8.49% and 47.4%.
Conclusion: Although current literature demonstrates inconsistency in the temporality of anosmia in patients diagnosed with COVID-19, the review was able to identify congruence points between the themes. Thus, enabling a better understanding of this symptom's progress, consequently raising pertinent questions with the need for further studies in order to improve medical conduct.
Disclosure: I have no potential conflict of interest pertaining to this submission.

EPO-053

Impact of the COVID-19 pandemic on the notification of neurological disease complications in Brazil

M. De Freitas [1], R. Simões Pissinatti [2], G. Moraes [2], T. Rodrigues Dias da Silva [2], P. Araújo [3], A. Alves [4], R. Souza [2], F. Mesquita [2]
[1] DSA, Lavras, Brazil, [2] Lavras, Brazil, [3] Bom Despacho, Brazil, [4] Belo Horizonte, Brazil

Background and aims: Until the 1st week of January / 2021, Brazil is the 3rd country with the highest number of confirmed cases of Coronavirus Disease – 2019 (COVID-19). Annually, neurological diseases and their complications culminate in approximately 200,000 hospitalisations in the Brazilian public health system. This work intends to investigate the relation between COVID-19 and its effect on the condition of neurological patients.
Methods: The research used the descriptors: Coronavirus Infections, Brazil, Nervous System Diseases; in PubMed, Scielo and Virtual Health Library databases. Through DataSUS, epidemiological data was collected about: Parkinson's disease, Multiple Sclerosis and Epilepsy.
Results: It was expected an increase in urgent hospitalisations related to the neurological diseases scanned. According to studies carried out in other countries, the exacerbation of neurological symptoms is possible. Contrariwise, there was a significant reduction in hospitalizations related to these diseases (DataSUS), especially between April and October 2020, when the number of COVID-19 cases increased dramatically in Brazil. The cause of reduction in hospitalisations may come from a scenario of systematic underreporting triggered by the pandemic. Hospitalisation due to coronavirus infection, in the Brazilian context, allows complications of pre-existing neurological diseases, resulting from COVID-19, to not be properly registered and notified in the integrated system.



Number of emergency neurological admissions – 2016 to 2020

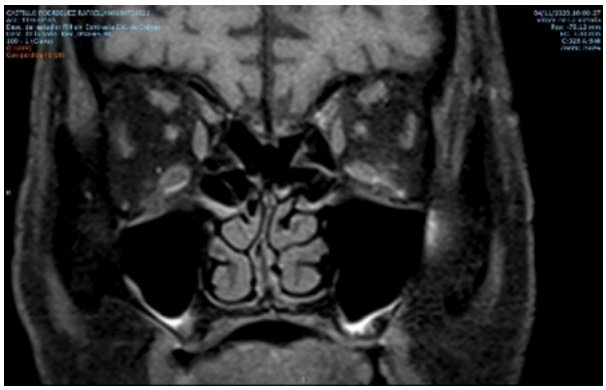
Conclusion: Brazil, due to its integrated health system, is able to provide full data collected from all its territory. Had there not been a noticeable reduction in hospital care due to fear of infection, this would enable further research and understanding of the effects of COVID-19 on pre-existing neurological conditions.
Disclosure: Nothing to disclose.

EPO-054

Diplopia due to SARS-CoV-2 swab test: a case report

I. De Laguno [1], C. De Rojas Leal [1], M. Mañez [2], O. Leon Plaza [2], O. Hamad Cueto [1]
[1] Neurology, Málaga, Spain, [2] Málaga, Spain

Background and aims: The current COVID-19 pandemic has made PCR nasopharyngeal swab test an essential procedure in both the screening and diagnosis of the general public and patients. Whereas there are many publications relating COVID-19 with a wide range of symptoms, complications/disorders related to testing are poorly described. Hence, we report a patient who developed diplopia after being tested with the nasopharyngeal swab test.
Methods: Case report
Results: A 63-year old man was admitted to the hospital to perform left fifth toe amputation due to diabetes-related foot complications. As part of our hospital protocol, a nasopharyngeal swab test was performed as COVID-19-screening-test, which resulted negative. A few hours later, the patient started complaining about left eye pain, exacerbated during eyeball movements, followed next day by double vision when looking down and to his right. Head CT-scan was unremarkable. The patient showed adduction, supra and infraduction paresis of the left eye, along with unilateral mild ptosis. A contrast head MRI showed a focal increase of left extraconal fat adjacent to the oblicous muscle and in contact to left nasal fossa roof, suggesting an orbital haematoma as the most plausible cause of the 3rd left cranial nerve palsy. The symptoms, diplopia and left eye pain, recovered partially with 50mg oral prednisone.



Conclusion: To our knowledge, this is the 1st reported case associating nasopharyngeal swab test, a method for COVID-19-screening-test, with diplopia. Therefore, in addition to medical conditions due to COVID-19 disease, physicians should be aware of complications related to PCR nasopharyngeal swab test.
Disclosure: Nothing to disclose.

EPO-055

Coronavirus and nervous system: what is the relationship?

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Background and aims: Coronavirus disease 2019 (COVID-19) was thought to cause a respiratory disease, sparing the other organs such as the nervous system. However, many patients developed a variety of symptoms suggesting the neurotropism of the virus.
Methods: Patients diagnosed with COVID-19 who developed neurological symptoms during the infection or afterwards were included in our study.
Results: Case1: A 52-year-old female presenting protein S deficiency and superficial venous thrombosis developed motor deficit and a confusional state. Her brain MRI showed multiple ischemic strokes. Case2: A 35-year-old man with familial history of epilepsy and psychomotor retardation, with personal history of pulmonary tuberculosis, glue sniffing and ethylism was admitted for psychiatric symptoms followed by tetraparesis. His brain MRI showed confluent hyperintensities of white matter and his electromyogram revealed a demyelinating polyneuropathy. Case3: A 69-year-old man admitted for multiple cerebral hematomas with altered state of consciousness and respiratory depression probably worsened by the infection Case4: A 32-year-old man developed three weeks after COVID-19 infection a seizure in context of apyrexia. His brain MRI was normal, his electroencephalogram showed a bifrontal slowdown activity.
Conclusion: Different mechanisms are thought to explain neurological manifestations in COVID-19 infection. Direct involvement of the nasal epithelium is responsible for the largely described anosmia. Ischemic stroke is related to the hypercoagulability and cardio-embolic complications. Confusional state is not related with infectious encephalopathy as suspected but to the influence of hypoxia, endothelial dysfunction and microthrombi. Peripheral nervous system involvement is less reported but many cases of Guillain Barré syndrome and myositis were reported.
Disclosure: Nothing to disclose.

EPO-056

Delirium in COVID-19 patients admitted to an Infectious Diseases Intensive Care Unit

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Background and aims: COVID-19 is a respiratory disease caused by SARS-CoV-2. Nevertheless, neurological complications have been described. Delirium, seems frequent, prolonged, and difficult to control.

Methods: To evaluate the prevalence and characteristics of delirium in a cohort of critically ill patients with COVID-19, compared to a historical cohort of critically ill patients with other respiratory infections. Retrospective comparative analysis of demographic, clinical and laboratory data from two cohorts: patients admitted to an Infectious Diseases Intensive Care Unit (IDICU) with COVID-19 and for other respiratory infections in 2018–2019. Olanzapine equivalent dosages of antipsychotics necessary to control delirium was used as a severity marker.

Results: We included 114 patients (74 COVID-19 and 40 non-COVID-19). The COVID-19 cohort presented with a statistically significant higher median age of 67 years old and a slight male predominance (56.8%). Previous neurological disease was present in 12.2%. Delirium developed in 45.9% of which, lasted a median of four days and needed a median of 10mg/day of olanzapine equivalents to control. Samples were matched to sex, previous neurological disease and use of benzodiazepines/antipsychotics. There was no difference in prevalence of delirium or its duration between cohorts ($p>0.05$). In patients with delirium the univariate analysis demonstrated a difference in the severity of delirium ($p=0.045$). In a model of multiple logistic regression, COVID-19 was associated with increased severity of delirium ($p\leq0.001$) adjusted for confounding factors.

Conclusion: COVID-19 is not associated with higher prevalence or duration of delirium. However, it seems to be associated with severe forms with increasing doses of antipsychotics needed its control.

Disclosure: Nothing to disclose.

Epilepsy 1

EPO-057

Seizures as a 1st manifestation of Anti-N-methyl-D-aspartate receptor encephalitis after ovarian teratoma removal

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Background and aims: Anti-N-methyl-D-aspartate receptor encephalitis (Anti-NMDARE) is an increasingly recognized, potentially lethal syndrome of psychiatric and neurological dysfunction which includes seizures in young patients, who have an underlying tumor. We present the challenges involved in its diagnosis and management.
Methods: The case of a 28 year old female, hospitalized after two focal seizures, with impaired awareness and evolution to bilateral tonic-clonic, 1st life event, without previous neurological, psychiatric pathology or seizures. Prior to admission, she was discharged from the gynecology department after a laparoscopic right ovarian cystectomy.
Results: At admission she was afebrile, without focal neurological deficits or meningeal signs. Paraclinical and imagistic without abnormalities, only focal left slowing on electroencephalography and at histology – mature ovarian teratoma. During the hospitalization she developed psychiatric symptoms (confusion, self-aggression, hallucinations), orofacial dyskinesias and involuntary movements of the upper extremities which progressed to catatonia, requiring specialized treatment in the psychiatric hospital. Preventively we collected serum ´Anti-NMDAR antibodies. Following a positive result, she was readmitted, performed an EEG, excluded the delta brush pattern or non-convulsive seizures; brain and pelvic MRI was without changes. Initiated specific treatment – plasmapheresis, with improvement of the psychoneurological condition, and antiepileptic drugs, followed by oral corticosteroids.

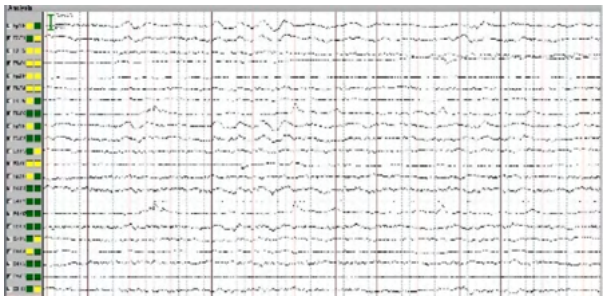

Fig.1. Video-EEG. Bipolar montage. Focal left F T slowing during sleep.

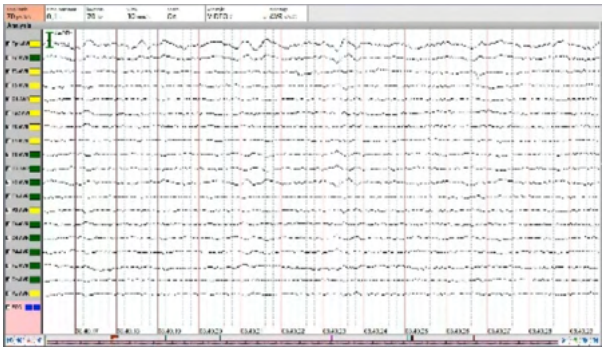

Fig.2. Video-EEG. Referential montage. Focal left F T slowing during sleep.

Analysis	Result	Unit	Ref.Range	GOÄ
1 Serum from 22.05.2019				
NMDAR AAB	↑ 1: 160		1: < 10	

Fig. 3. Anti-NMDA-R antibodies result

Conclusion: Anti-NMDARE is a challenging condition, requiring greater emphasis of clinical and paraclinical manifestations, antibodies determination in order to prevent misdiagnosis. This case illustrates the importance of suspecting an autoimmune encephalitis even if the ovarian teratoma was removed and symptoms do not follow a strict phase progression and the results of antibody testing are delayed.
Disclosure: Nothing to declare.

EPO-058

Abstract withdrawn

EPO-059

Sporadic Nocturnal Frontal Lobe Epilepsy: About three cases

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Background and aims: Sporadic Nocturnal Frontal Lobe Epilepsy (NFLE) is a rare form of epilepsy that has been infrequently reported, in contrast to Autosomal Dominant Nocturnal Frontal Lobe Epilepsy (ADNFLE).
Methods: Three consecutive cases of sporadic NFLE were evaluated at CHU Habib Bourguiba, Sfax. All patients had clinical interviews (age of onset of epilepsy, the semiology of the epileptic seizures and the antiepileptic treatment), neurological examinations, EEG and brain MRI.
Results: There were two men and a woman. Premorbid history was negative for any neurologic or psychiatric disorder. All patients had NFLE,without any positive family history. The mean age of NFLE onset was 17.33 years (±4.6 years). NFLE subtypes: nocturnal paroxysmal dystonia for two patients and paroxysmal arousals for the last one. The neurological examination and the brain MRI were normal. Only one patient showed focal frontal epileptic abnormalities on EEG. No case had a spontaneous remission. Carbamazepine was highly effective in all cases. NLFE is a rare form of epilepsy. The average age of onset of this epileptic syndrome is 18.4 years (17.33 years in our series). In accordance with the data in literature, our patients presented several seizures per night with predominant motor manifestations. There was a high rate of sustained anticonvulsant treatment efficacy, particularly with carbamazepine.
Conclusion: NLFE is a rare condition that begins at an early age. Our findings reinforce the fact that this epilepsy should be suspected in the presence of paroxysmal nocturnal motor events.
Disclosure: My research has not been granted by any commercial or institutional support.

EPO-060

Nocturnal abnormal EEG, seizure control and polysomnographic variables among epilepsy patients

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Background and aims: Epilepsy is one of the most prevalent noncommunicable neurological disorders worldwide. Sleep plays an important role in patients with epilepsy (PWE) and its disturbance/poor quality can impact the seizure control. We aimed to explore the impact of the presence of nocturnal EEG abnormalities on seizure control and polysomnography-(PSG)-derived sleep pattern among PWE.
Methods: Patients with focal and generalized epilepsy were included. Each underwent a combined EEG/PSG study and information about seizure frequency during last month (SFDLM) and last year (SFDLY) was obtained. Based on presence and absence of nocturnal EEG abnormalities the participants were separated into two groups: Non-ABNEEG and ABNEEG. Mann-Whitney U test was used for statistical analysis.
Results: Sample descriptives: n=85, mean age – 35.1(18–69), F/M=50.6%/49.4%. The data on EEG abnormalities, seizure frequency and PSG findings are presented in Table 1. There was significant difference between the presence of nocturnal abnormal EEG and SFDLY; SFDLM; wake time; total sleep time; number of awakenings at night ($p<0.05$), whereas it was found to be non-significant between EEG abnormality and apnea-hypopnea index; oxygen-desaturation index; periodic limb movement index (PLMI) ($p>0.05$).

Variable	Means		p-value
	Non-EEG abnormality group (n=17)	EEG abnormality group (n=68)	
SFDLY	6.35	48.09	p<0.05
SFDLM	0.764	5.25	p<0.05
Wake time	82.28	63.09	p<0.05
Total sleep time	408.32	438.02	p<0.05
Awakenings at night were	14.94	9.43	p<0.05
Apnea-hypopnea index	5.69	6.22	p>0.05
Oxygen-desaturation index	5.81	6.93	p>0.05
PLMI	5.99	5.54	p>0.05

Table 1. EEG abnormalities, seizure frequency and PSG findings for Non-ABNEEG and ABNEEG groups.

Conclusion: Our data suggest that nocturnal abnormal EEG may be connected to poor seizure control among epilepsy patients. Sleep structure was better in ABNEEG, while the pathological PSG findings were not different between PWE with and without nocturnal abnormal EEG. As the role of sleep among epilepsy patients is underestimated, clinicians need more studies addressing the impact of sleep on seizure control and patient outcomes.
Disclosure: Nothing to disclose.

EPO-061

Pediatric Symptomatic Epilepsy: Etiological Spectrum and Radio Electroencephalographic Correlation

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Oujda, Morocoo

Background and aims: Symptomatic epilepsy refers to epilepsy secondary to an underlying condition. An acute analysis of clinical features and specific investigations especially brain magnetic reasoning imaging (MRI) and electroencephalogram are necessary to establish the etiology of epilepsy. The aim of our study is to analyze the clinico-radiological profile of symptomatic pediatric epilepsies and to study the correlation between radiological and electroencephalographic data.
Methods: This is a retrospective study on the medical file of 75 children with epilepsy examined by brain MRI, collected at the neurology and radiology departments of the Mohammed VI University Hospital of Oujda, during a period from September 2015 to November 2020. All patients benefited of rigorous clinical examination, brain MRI, electroencephalogram.
Results: Our study included 75 children, with an average age of six years (11 months – 15 years). The sex ratio was 1,14. 24% of our patients presented drug-resistant epilepsy. The epileptogenic lesions found are in decreasing order of frequency: perinatal anoxo-ischemia lesions (32%), cerebral malformations (20%), after-effects of trauma (12%), cerebral-meningeal infections (12%), mesiotemporal sclerosis (8%), tumors (8%), metabolic (4%), and vascular malformations (4%). The correlation between radiological and electro-encephalographic data was found in 84% of cases.
Conclusion: MRI is imaging modality of choice for exploring symptomatic epilepsy. The precision of the localization of the epileptogenic focus is increasingly possible, due to the optimal use of new imaging techniques, allowing a good clinical-radio-electroencephalographic correlation.
Disclosure: Nothing to disclose.

EPO-062

Evolution of old-generation antiepileptic drugs usage in patients with drug resistant epilepsy

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Background and aims: In the 21st century, the list of antiepileptic drugs has significantly expanded, new drug generation become actively involved in epilepsy management, which affects the prevalence of the old-generation drugs in medical practice. Our objective was to study evolution of old-generation antiepileptic drugs in the 20th and 21st century.
Methods: We studied medical history of antiepileptic therapy in 60 neurosurgical patients with drug resistant epilepsy at Polenov Neurosurgical Institute in 2020. We divided them in two groups: group 1 consisted of patients with disease onset in the 20th century (duration of their disease was over 20 years) and group 2 was comprised of patients with epilepsy onset in the 21st century (disease duration –less than 20 years) and compared the frequency of old-generation medicine in the groups. The method of descriptive statistics was used.
Results: The number of patients in group 1 was 32, in group 2 – 28 respectively. The sex ratio was one male to one female. In group 1 old-generation drugs in the anamnesis comprised 61%, in group 2 – 42 % (p=0.05). Barbiturates – 21% and 5%, Benzodiazepines – 5% and 0%, Valproates – 15.4% and 20%, Carbamazepines –15% and 15.5%, respectively.
Conclusion: We have noted a significant decrease in the use of old-generation drugs versus new generation ones in epilepsy in the 21st century, mainly through a decrease of the prevalence of bariturates and benzodiazepines. Valproates and carbamazepines continued to be used in epilepsy management in the 21st century.
Disclosure: Nothing to disclose.

EPO-063

Transient lesions on brain MRI after epileptic seizures

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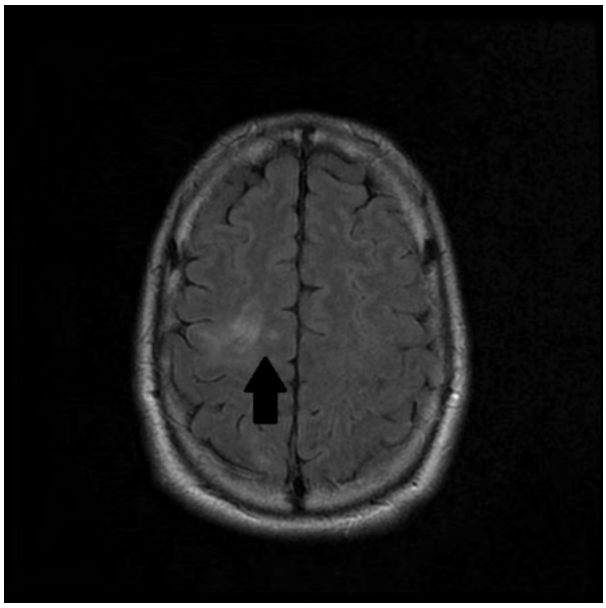
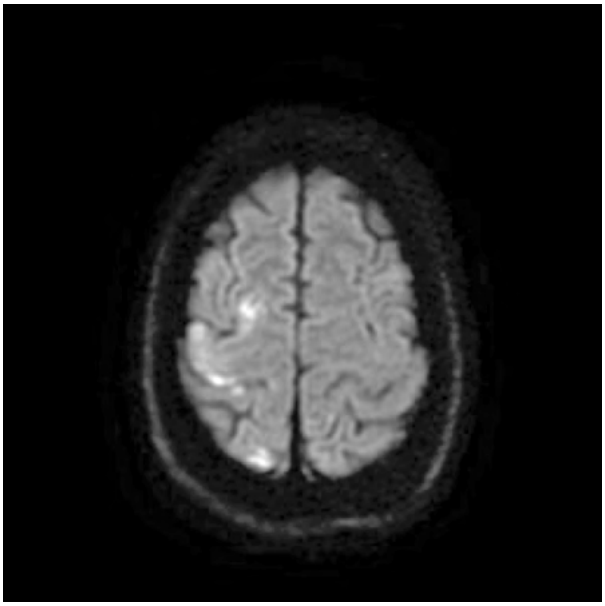
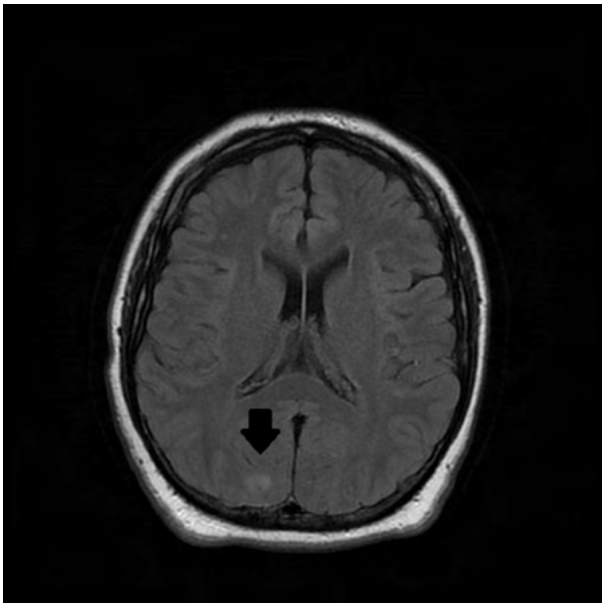
Background and aims: Epileptic seizures can cause transitory alterations at the cerebral level, it`s very important to detect these lesions to avoid invasive procedures. In the literature, they are described frequently in cases of status epilepticus, although they also appear in isolated seizures.
Methods: We present a case of status epilepticus and another of isolated epileptic seizures with transient alterations in brain magnetic resonance imaging (MRIb).
Results: 1st Case: 48-year-old man with a history of secondary generalized focal epilepsy with previous MRIb and EEG normal. He has been presenting focal seizures for 10 hours consisting of clonic movements in the lower left limb. In MRIb was seen: signal alterations are observed at the cortico-subcortical level in the right hemisphere and the caudate nucleus left isointense in T1 and hypertensive in long TR, with diffusion restriction. In EEG postcritical there was epileptiform activity in the right temporal bone. At three weeks, the MRIb and the EEG were normalized. 2nd Case: 34-year-old man presented one focal visual seizures consisting of left palinopsia. In EEG there was no epileptiform activity. CMRI was performed with a hypersignal focus in the right occipital lobe in T2 and FLAIR with diffusion restriction. The control MRIb at two months was normal.



1st case: IRMb FLAIR



1st case: IRMb Diffusion



2nd case: IRMb FLAIR

Conclusion: Recognizing these lesions in patients who have suffered a seizure can avoid performing invasive procedures, the characteristics of the lesions are varied. We must carry out the control with MRIb to confirm the transience and benignity of the lesions, which can keep up to 12 months.
Disclosure: I have not received commercial or institutional support.

EPO-064

Abstract withdrawn

EPO-065

Long-term efficacy/safety of adjunctive eslicarbazepine acetate:open-label extension study in adults with focal seizure

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Background and aims: We evaluated long-term efficacy and safety of eslicarbazepine acetate (ESL) as adjunctive therapy for adults with focal seizures.
Methods: Open-label extension study in patients who completed a randomised, double-blind, placebo-controlled study (BIA-2093-304 Part I). Part II (1 year): starting dose of ESL 800mg/day, for one month, thereafter, dose individualized within 400–1600mg/day range. Part III (two years): starting dose of completion of Part II, with similar adjustments.
Results: Of 496 patients enrolled in Part II, 346(69.8%) completed, and 240 entered Part III(55(22.9%) completed). Mean CGI-S change from baseline (Part I) to end of Part II and end of Part III scores were -1.0(1.4) and -0.7(1.5). For completers, mean change in standardised seizure frequency from baseline to end of Part II was -5.8(18.6) seizures/28 days. Responder and seizure freedom rates were 40.0% and 9.6%. Mean overall seizure severity questionnaire score improved at all visits during Part II, compared with baseline. Treatment-emergent adverse events(TEAEs) were reported by 75.4% (n=361, Part II) and 68.5% (n=152, Part III) of patients. Most frequent possible related TEAEs were dizziness (16.7%), somnolence (7.7%) and diplopia (7.5%) in Part II and dizziness (5.9%) and headache (5.4%) in Part III. Most TEAEs were of mild or moderate intensity and just 6.5% lead to discontinuation in Part II and 3.2 % in Part III.
Conclusion: Long-term treatment with ESL in adult patients with focal seizures was associated with sustained therapeutic effect among those who had elected to remain in the study for additional open-label extensions and was generally well tolerated.
Disclosure: Work supported by BIAL- Portela & Ca, S.A., S. Mamede do Coronado, Portugal.

EPO-066

Treatment options for women with genetic generalized epilepsies

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Background and aims: Valproate (VPA) is the most effective drug for patients with genetic generalized epilepsies (GGEs). However it associated with a higher risk of structural and neurobehavioral teratogenicity in exposed offsprings and its use in women of childbearing potential has been recently restricted. The aim of our study was to investigate the pattern of treatment response in women with GGEs.
Methods: We retrospectively reviewed data from female patients with GGE followed at our center since 1999. Were evaluated remission rates with different types of antiseizure medication (ASM). Seizure remission (SR) was defined as the absence of any seizure type for at least 12 months at any time during follow-up.
Results: We included 123 women aged 32,7 years (SD± 9,7) with mean age of epilepsy onset 15,1 years (SD±5,1). 62 suffered from Juvenile Myoclonic Epilepsy, 30 from Juvenile/Childhood Absence Epilepsy and 27 from Generalized Tonic–Clonic Seizures Alone and five had others GGE syndromes. The majority of patients (99; 80,0%) have ever used VPA. A total of 87 (70,7%) have at least one year seizure free and 68 of these women were seizure-free on VPA. 42 (34%) were seizure free on other ASM, mostly on levetiracetam or lamotrigine. One 3rd (13; 31%) of seizure-free women were switched from VPA to other ASM. One 3rd of women who used VPA have never been switched to other AMS for different reasons.
Conclusion: At least one third of WOCP with GGEs may enter remission on ASM with low teratogenic potential.
Disclosure: MB received honoraria for publications from Sanofi; honoraria for lectures, travel expenses and conference fees from Sanofi, Adamed, Teva Pharmaceutical, Neuraxpharm, Glenmark, UCB Pharma.

EPO-067

Insular lobe epilepsy: challenges of diagnosis and management – a pathway to seizure freedom

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Background and aims: Insular cortex epilepsy is an increasingly highlighted and diagnosed type of intractable epilepsy. As the insular lobe has a great number of functions and a widespread network of connections, insular seizures feature various clinical manifestations. Rapid propagation to the contralateral insular cortex and to other neural hubs and the deep location of the insular cortex reduce the role of scalp electroencephalography (EEG) in the diagnostic process. Furthermore, patients often have normal structural brain imaging studies and functional imaging offers no clue whatsoever regarding lateralization.
Methods: We present a case series of patients with intractable insular epilepsy who had their presurgical work-up performed in our Epilepsy Monitoring Unit.
Results: Stereo-EEG unveiled anterior, middle and posterior insular cortex as main seizure generators. Functional cortex and ictal-implicated cortical areas were delineated by means of direct cortical electrical stimulation. We obtained synchronized video, scalp-EEG and stereo-EEG recordings. Correlations could thus be inferred based on electrical activity recorded by both scalp and depth electrodes regarding lateralization, order of hubs' involvement and their moment in time-locked expression as clinical feature. Thermocoagulation was performed as 1st step in disrupting the epileptogenic network with subsequent improvement. In patients with brain resection based on the presurgical work-up seizure freedom was achieved.
Conclusion: Non-invasive work-up in cases of insular epilepsy is rarely eloquent by itself. Invasive exploration based on careful electroclinical reasoning can help identify the epileptogenic network. Synchronized video, scalp-EEG and stereo-EEG recordings prove that every detail matters in solving intractable epilepsy cases, particularly involving deep and extensively connected brain hubs.
Disclosure: Nothing to disclose.

EPO-068

Epilepsy in Brazil, from 2010 to 2019: epidemiological profile and mortality in Brazilian macro-regions

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Background and aims: Studies indicate that 75% of people living with epilepsy in underdeveloped countries do not receive the necessary treatment, increasing the risk of premature death. Therefore, it is relevant to understand the epidemiological profile of hospitalisations due to epilepsy and its mortality rate in Brazil over the last decade.
Methods: Retrospective, ecological study accomplished through the Hospital Information System of the Brazilian Unified Health System (SIH/SUS/DATASUS), analyzing hospitalisations, macro-regions, mortality rate (MR), sex, age and skin colour.
Results: 507,440 hospitalisations for epilepsy were reported in Brazil from 2010 to 2019. The Southeast macro-region accounted for 44.7% of hospitalisations (n=226,572), followed by the South with 21.2% (n=107,613) and the Northeast with 20.8% (n=105,657). The highest MR was observed in the Northeast macro-region (MR=3.01) and the lowest in the South (MR=1.43). As for sex-wise, there was a higher prevalence of hospitalisations among men (58.0%; n=294,527), with their MR being higher than the Brazilian average rate (MR=2.25). A higher prevalence of hospitalisations in the age group from one to four and a lower prevalence among elderly people over 80 were noticed. There was a higher number of hospitalisations of white people (35.5%; n=180.010), followed by brown people (30.6%; n=155.030) and black people (3.8%; n=19.359).

	BRAZILIAN MACRO-REGIONS					TOTAL
	SOUTHEAST	SOUTH	NORTHEAST	MIDWEST	NORTH	BRAZIL
HOSPITALISATIONS 2010-2019, n (%)	226.572 (44,7)	107.613 (21,2)	105.657 (20,8)	40.797 (8,0)	26.831 (5,3)	507.440 (100)
MORTALITY RATE	2,45	1,43	3,01	2,42	1,97	2,25

Source: Hospital Information System of the Brazilian Unified Health System (SIH / SUS / DATASUS).

Hospitalisations and mortality rate due to epilepsy in Brazil and its macro-regions, from 2010 to 2019.

Source: Brazilian Institute of Geography and Statistics (IBGE), 2021.

Regional division of Brazil into macro-regions.

Conclusion: In Brazil, over the last decade, there was a higher prevalence of hospitalisations for epilepsy among white children, aged one to 4, living in the Southeast macro-region. However, the mortality rate in the Northeast was higher than in the other Brazilian macro-regions.
Disclosure: There are no conflicts of interest.

EPO-069

Sporadic Creutzfeldt-Jakob presenting as epilepsia partialis continua

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[1] Lisboa, Portugal, [2] 1- Neurology, Department of Neurosciences and Mental Health, Hospital de Santa Maria, Centro Hospitalar Universitário Lisboa Norte, Lisbon, Odivelas, Portugal, [3] 1- Serviço de Neurologia, Departamento de Neurociências e Saúde Mental, Hospital de Santa Maria, Centro Hospitalar Universitário Lisboa Norte, Lisboa, Lisboa, Portugal, [4] Neurologia, Lisboa, Portugal, [5] Neurology Department, Lisboa, Portugal

Background and aims: Epilepsy is a well-known manifestation of Creutzfeldt-Jakob disease (CJD), mostly identified in its end-stages. Seizures as a presenting feature is rare.
Methods: We report a CJD case presenting with epilepsia parcialis continua (EPC).
Results: A 72-year-old male presented with a 1-month history of cognitive decline, left side weakness, gait instability, and left hand stereotyped involuntary movements. Neurological examination revealed left hand myoclonic jerks, ipsilateral hemiparesis and hemiataxia, and brisk osteotendinous reflexes. Initial blood tests and CSF were unremarkable (serological and microbiological exams, autoimmune and antineuronal antibodies). Brain MRI showed right DWI sequence fronto-insular and parieto-occipital cortical hyperintensities. EEG disclosed periodic epileptic discharges in right centre-parietal regions, establishing an EPC diagnosis. Antiepileptic drugs (AEDs) were started. Myoclonic jerks improved, maintaining a similar EEG. One month later, neurological deterioration was noted, with cognitive impairment, appendicular cerebellar ataxia, axial instability, aggravated left hemiparesis, maintaining left hand myoclonic jerks. AEDs' adjustment led to a slight clinical improvement. Follow-up EEG maintained periodic lateralized epileptic discharges at 1–1.5 Hz, primarily at right centre-parietal regions, synchronous with myoclonic jerks. Protein 14-3-3 was CSF positive. No pathological PRNP gene mutations were found, with a MV heterozygosity at codon 129. Re-evaluation brain MRI showed DWI sequence bilateral cortical hyperintensities, and the EEG pattern evolved to generalized periodic sharp wave complexes at 1Hz, establishing a probable sporadic CJD diagnosis.
Conclusion: Remember to consider CJD in EPC patients, especially when associated to other symptoms or refractory to AEDs. Another five cases of EPC-presenting CJD have been previously described.
Disclosure: Nothing to disclose.

Headache and Pain 1

EPO-070

Polymorphisms of thrombophilia genes in patients with reversible cerebral vasoconstriction syndrome

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Background and aims: Reversible cerebral vasoconstriction syndrome (RCVS) characterized by the acute intense headache, focal and/or universal cerebral symptoms, epileptic paroxysms, accompanied by reversible segmental multifocal cerebral vasospasm, which disappears in three months. Course of RCVS may be complicated by cerebral edema,ischemic and hemorrhagic strokes.Aim of our study was to identify gene polymorphisms predisposing to hereditary thrombophilia in RCVS patients.

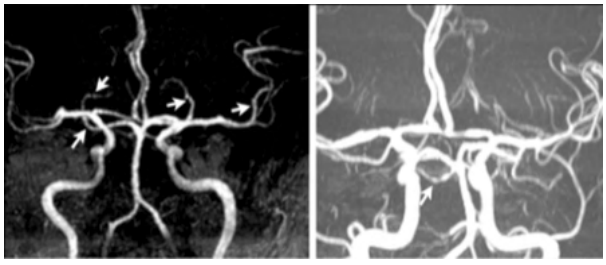

Figure 1

Methods: 24 patients (age 38±11 years) with RCVS were examined: 19 women (79.1%) aged 38.0±11.4 years,5 men (20.8%) aged 38.2±11.3 years.There didn't find significant gender difference in age. Investigation included routine clinical and neurological examination,neuroimaging research methods (brain MRI on 1.5T or 3T, MR arteriography) and molecular genetic study of polymorphisms predisposing to thrombophilia: G20210A of prothrombin gene,C677T methylenetetrahydrofolate reductase gene, 675 4G/5G gene of endothelial plasminogen activator inhibitor (PA1-1, SERPINE1), 455 G/A gene of the beta-polypeptide chain of fibrinogen

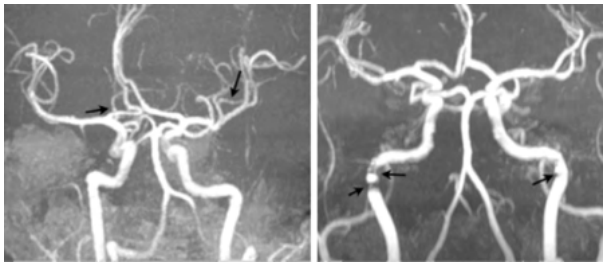

Figure 2

Results: Polymorphism G20210A in the prothrombin gene was not detected in the examined patients. Heterozygous carriage in the methylenetetrahydrofolate reductase gene was observed in 10 patients – in nine women and one man (43.5%), homozygous-in two women (8.3%). Polymorphism of the endothelial plasminogen activator inhibitor gene was detected in 16 patients (12 women and four men) in the heterozygous state (66.7%) and in three – in the homozygous state (12.5%). Polymorphism 455 G/A was detected in heterozygous state in six patients (25%): five women and one man and in homozygous state in four patients(16.7%) – two women and two men.

Conclusion: The role of the revealed changes in the development of the complicated course of RCVS requires further study. A molecular genetic study of hereditary thrombophilia in patients with RCVS revealed polymorphisms of following genes: endothelial plasminogen activator inhibitor, methylenetetrahydrofolate reductase and fibrinogen.

Disclosure: Nothing to disclose.

EPO-071

Factors determining the response to treatment in patients with vestibular migraine

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Background and aims: Studies investigating factors that affect the response to treatment in patients with vestibular migraine (VM) is sparse.
Methods: Patients diagnosed as VM and treated with agents recommended in migraine prophylaxis were included in this multicenter study performed in eight tertiary Neurology clinics. Migraine features including type, age of onset of headache and vertigo attacks, headache and vertigo attack duration, intensity, associated symptoms, triggering factors, presence of interictal dizziness/imbalance, anxiety, depression, history of motion sickness, family history of migraine were noted. Agents used for treatment included amitriptyline, flunarizine, propranolol, topiramate and venlafaxine. 50% reduction in attack frequency and severity in patients using one drug, and a combination of two drugs of different class was compared with patients showing <50% reduction despite combination therapy, regarding their clinical features.
Results: The results gathered from 430 VM patients, 65 men (15%) and 365 women (85%) with a mean age of 42,2±12,2 years (range: 17–74 years), were analyzed. Logistic regression analysis revealed female sex, associated allodynia and aural fullness, presence of interictal dizziness/imbalance, comorbid anxiety and depression were significantly associated with poor response to treatment.
Conclusion: Cutaneous allodynia frequently associated with being female and comorbid anxiety and depression, interictal dizziness/imbalance enhanced with comorbid anxiety came all together to end up with reduced treatment response. Aural fullness can be the clue of impending concomitant Meniere's disease not expected to respond to migraine preventives.
Disclosure: Nothing to disclose.

EPO-072

Vestibular migraine, demographic and clinical features of 415 patients: a multicenter study

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Background and aims: To evaluate clinical features in vestibular migraine (VM).
Methods: A cross-sectional, multicenter study was performed in eight tertiary Neurology clinics.
Results: 415 VM patients were studied. Mean age of headache onset was 25 years, vertigo onset was 39 years. In 38% temporal association of vertigo and headache was present in less than 50% of the attacks. 10% had hearing loss on audiometry, in 8.7% it was typical for Meniere's disease (MD). Median headache attack severity assessed by VAS was eight and vertigo attack severity was 7. In patients under 43 years of age headache attack severity was significantly high whereas in patients over 41 years of age vertigo attack severity was high. In 61.9% anxiety was present and in 51.8% motion sickness was revealed from past medical history. Similar headache attacks were present in 72.5% and vertigo attacks in 29.2% of the family members. In patients with a positive family history, age of onset of both migraine headaches and vertigo attacks was low. During the interictal period typical posterior canal benign paroxysmal positional vertigo (BPPV) type positional nystagmus was detected in 12.3%.
Conclusion: VM was associated with MD in 8.7% and BPPV was present in 12.3%. Headache severity was high in younger patients whereas vertigo attacks were more severe later in life. A positive family history was associated with lower age of onset of both headache and vertigo attacks. History of motion sickness was very common and anxiety disorder was a frequent comorbidity.
Disclosure: Nothing to disclose.

EPO-073

Prevalence and severity of headache in medical students during quarantine due to COVID-19

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Background and aims: Headache is among COVID-19-related frequent symptoms. Quarantine triggers psychological disturbances.
Methods: We administered in September-November 2020 an online, self-reported survey, that included demographic data, characteristics and course of headaches in medical students during quarantine, as well as the connection with COVID-19.
Results: A total of 447 students (327 (73.2%) females, mean age of 21.7±3.6 years) contributed to the survey. According to the survey results, 86.9% students suffered from headaches. Of these, 74.2% students had headaches 1–7 days a month. Students associated the onset of headaches with increased anxiety (51.0%), on-line university study (34.5%), excessive time spent at the computer (49.0%), decreased physical activity (26.5%).
The pain mainly had bilateral localization (80.9%), moderate intensity (54.4%) and duration up to 12h (77.3%). 31.7% students reported the increase of the headache frequency and 26.3% – increase of the headache severity during quarantine. 74 students suffered from COVID-19. COVID-19 related headaches were more closely associated with anosmia/ageusia ($p<0.05$). Logistic regression analyses showed that bilateral tension headache, duration over 24h, male gender were significant variables to differentiate COVID-19 positive patients from those without COVID-19 ($p<0.05$). Severity of headache during COVID-19 increased in 37.8%, after COVID-19–in 24.3% students.
Conclusion: There is a high prevalence of headaches among medical students, which is associated with different psychological stressors during quarantine and on-line university study. Bilateral tension headache with duration over 24h, male gender are characteristics of COVID-19 headaches, as well as in combination with anosmia/ageusia. COVID-19 has a negative effect on the severity of headaches, even in young patients.
Disclosure: Nothing to disclose.

EPO-074

Central sensitization -the main mechanism of comorbidity of migraine and endometriosis.

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Background and aims: Migraine and endometriosis are comorbid conditions, but the mechanisms of their comorbidity have not been fully understood. The aim of our study was to analyze the characteristics of the pain syndrome in patients with migraine and genital endometriosis, to find out the mechanisms of their comorbidity.
Methods: 125 patients who visited a gynecologist for endometriosis were examined for migraine. 79 patients with laparoscopically confirmed diagnosis of genital endometriosis participated in the study and two age-matched groups were formed: the main group-38 patients with endometriosis and migraine, the comparison group-41 patients with endometriosis without migraine. All patients were given clinical neurological study, an evaluation of pelvic pain by the pelvic pain index, and determination of the level of central sensitization(CS) using the Central Sensitization Inventory(CSI).
Results: 42.4% of 125 patients with endometriosis, suffered from migraine, which confirms the comorbidity of these diseases. Chronic pelvic pain (CPP), dysmenorrhea, dyspareunia, and dyschezia were more common among the patients of the main group; the comparison group had more patients withut pelvic pain symptoms. A significantly higher level of CSI and pelvic pain index had the patients with migraine and endometriosis compared to patients with only endometriosis(Tab.1). We did not find also significant difference between the forms of endometriosis in the two groups (Fig.1). The severity of pelvic pain did not correlate with the form of endometriosis, which demonstrates the important role of central neurogenic mechanisms in the pathogenesis of pain in the comorbid diseases.

Feature	Main group (Migraine+Endometriosis) (n=38)	Comparison group (Endometriosis) (n=41)	p
Dysmenorrhea, %:	97,3%	65,86%	0,001

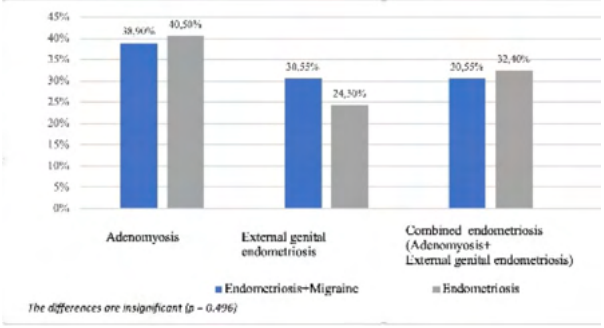

Fig.2.The prevalence of different forms of endometriosis.

Conclusion: Central sensitization is the main mechanism of comorbidity of migraine and endometriosis.
Disclosure: No authors have a financial or property interest in any material or method mentioned. There is no conflict of interests.

EPO-075

Pharmacological treatments in migraine patients: an overview from a tertiary headache centre

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Background and aims: Headache prevention and level of management can be challenging. Aim of the present study was to assess efficacy and side effects of migraine preventive therapies and to characterize the clinical pertinence of patients being addressed to a tertiary Headache Centre.
Methods: Patients visited at the Headache Centre of Spedali Civili of Brescia with a diagnosis of primary headache during September-November 2020 were included. Descriptive statistical analyses were performed. Information regarding headache diagnosis and frequency, disease duration, number and type of previous/ongoing symptomatic and preventive therapies were collected.
Results: 320 patients were enrolled, of which 146 1st-time users and 174 follow-up patients. Demographic and clinical characteristics are presented in Table 1. As presented in Table 2, mean monthly headache days in 1st-time users were high, even in patients with a diagnosis of episodic migraine. All patients who presented to our Centre, with a diagnosis of tension-type headache, demonstrated a chronic frequency. Considering all migraine patients (n=202), the most frequently used oral preventive therapies were amitriptyline and topiramate (Figure 1), which also showed the highest rates of adverse events and efficacy.

	FIRST-TIME USERS (n=146)	FOLLOW-UP PATIENTS (n=174)
AGE, years (mean, SD)	41.2 (15.1)	44.9 (13.2)
GENDER, F (n,%)	108 (73.9%)	139 (79.8%)
DISEASE DURATION, years (mean, SD)	16,6 (12.3)	21.7 (13.7)
DIAGNOSIS (n, %)		
EPISODIC MIGRAINE	82 (56.2%)	64 (36.9%)
CHRONIC MIGRAINE	18 (12.3%)	88 (49.9%)
TENSION TYPE HEADACHE	41 (28.1%)	21 (11.6%)
CLUSTER HEADACHE	5 (3.4%)	1 (0.6%)
MEDICATION OVERUSE (n, %)	4 (2.7%)	70 (40.2%)
PREVIOUS PROPHYLAXYS		
NONE (n, %)	98 (67.2%)	40 (23.1%)
1-2 (n, %)	39 (26.7%)	73 (41.9%)
> 2 (n, %)	9 (6.1%)	61 (35%)
ACUTE TREATMENTS		
OTC NSAIDs (n, %)	110 (75.4%)	52 (30%)
TRIPTANS (n, %)	35 (23.9%)	120 (68.9%)
COMBINATION ANALGESICs (n, %)	1 (0.7%)	2 (1.1%)

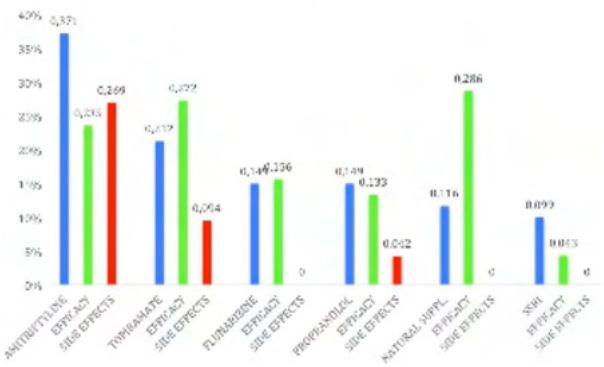
SD: standard deviation; n: number; OTC: over-the-counter; NSAIDs: non steroidal anti-inflammatory drugs.

Clinical and demographical characteristics of all subjects

	FIRST-TIME USERS (n=146)	FOLLOW-UP PATIENTS (n=174)
HEADACHE DAYS/MONTH (mean, SD)		
EPISODIC MIGRAINE	8.1 (7.7)	6.01 (5.2)
CHRONIC MIGRAINE	21.1 (7.7)	15.2 (6.7)
MEDICATION OVERUSE	18.8 (8.2)	14.4 (4.8)
TENSION TYPE HEADACHE	15.3 (12.6)	6.8 (4.4)

SD: standard deviation.

Headache frequency, according to the headache diagnosis, in all subjects



Rate of utilization, efficacy and adverse events of oral preventive therapies in all migraine patients

Conclusion: Considering diagnosis, headache frequency and duration, previous treatment failures and acute treatments, our cohort documented a high burden of disease and disability, with a correct indication to a tertiary level Headache Centre. Migraine oral preventive therapies did not show a satisfactory effectiveness, mostly associated with moderate-to-high rates of adverse events. In this scenario, more specific and effective treatments (Onabotulinumtoxin-A and monoclonal antibodies targeting CGRP) are a promising therapeutic alternative.
Disclosure: The authors have nothing to disclose.

EPO-076

INFLUENCE OF PAINKILLERS IN MEDICATION OVERUSE HEADACHE

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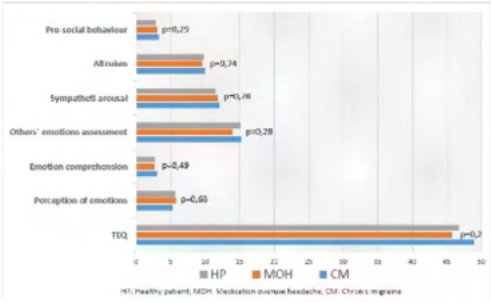
Background and aims: In recent years, the effects of painkillers on empathy have been studied showing their influence on empathy. This topic has not been studied yet in patients with medication overuse headache (MOH). The aim of this study is to evaluate the empathy in patients with MOH and comparing them with patients with chronic migraine (CM) and healthy people (HP) using the Toronto Empathy Questionnaire (TEQ).
Methods: Data of age, sex and diagnosis were collected. All patients filled the TEQ which allows us to evaluate empathy as well as the perception of emotion, emotion comprehension, assessment of emotions, sympathetic arousal, altruism and pro-social behaviour. General Anxiety Disorder Questionnaire (GAD7) was also filled by all patients.
Results: The mean age was 42±11,54 years-old. 50 patients were collected, 34 women (66,7%), 16 men (31,3%). 15 (29,4%) had MOH, 18 CM (35,3%) and 17 HP (33.3%). TEQ had a mean of 45,7±4,8 in MOH, 49±6,3 in CM and 46,8±4 in HP (p=0.2). Mean values of perception of emotion, emotion comprehension, assessment of other´s emotions, sympathetic arousal, altruism and pro-social behaviour did not show statistical differences amongst three groups. Mean GAD7 scores in MOH, CM and HP were 10,4±3,6; 8,7±4,6 and 5,59±3,4 respectively (p=0.04).

		GENDER			TORONTO EMPATHY QUESTIONNAIRE						
	n	Male	Female		TEQ (Total)	Perception of emotions	Emotion comprehension	Others' emotions assessment	Sympathetic arousal	Altruism	Pro-social behaviour
CM	18 (36%	4	11		49	5,27	3	15,1	12,13	10	3,27
MOH	15 (30%)	5	13		45,78	5,72	2,67	13,94	11,78	9,56	3
HP	17 (34%)	7	10		46,82	5,65	2,76	15,12	11,53	9,82	2,82
TOTAL	50 (100%)	16	34	P value	0,2	0,65	0,49	0,28	0,78	0,74	0,29



Conclusion: Our findings did not show any statistical difference in all explored aspects of empathy with the TEQ amongst all groups. However, we encourage to study further in order to look for any effect of pain killers in empathy amongst MOH and CM.
Disclosure: Nothing to disclose.

EPO-077

High Riding Jugular Bulb: another cranial venous anomaly causing headache

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Background and aims: Headache associated with pulsatile tinnitus is indicative of a potential secondary headache and requires an etiological study.
Methods: Case report
Results: A 35-year-old woman was referred to a neurology consultation for headache. The onset of episodes occurred during pregnancy, with right pulsatile hemicranial headaches, associated with photophobia and vomiting and lasting about 24 hours. The neurological examination was unremarkable. She performed cranioencephalic MR with an arterial angiographic study that did not reveal any pathological changes. After a few months, the patient recurs with worsening complaints: a more frequent self-audible pulsatile bruit on right ear, which is not always associated with headache but is correlated with postural changes. She denied other hearing complaints and otoscopy did not reveal any changes. A CT Venography was performed, showing a high right jugular bulb, that insinuated into the hypotympanum, without bone disruption. There was no signs of venous thrombosis or venous dural stenosis, namely involving the transverse sinus.
Conclusion: High Riding Jugular Bulb is mostly asymptomatic, being usually an incidental finding on CT; however it may present with dizziness, conductive-type hearing loss and headache with pulsatile tinnitus. As seen in this case, it can become symptomatic in high cardiac output states (such as pregnancy). Although the International Classification of Headache Disorders does not address this venous cause of headache, this aetiology should be considered in cases of headache associated with pulsatile tinnitus. There is still no consensus regarding the treatment of this entity but there are some reports of surgical or endovascular treatments with good outcomes.
Disclosure: Nothing to disclose.

EPO-078

Improved patient engagement in mobile health solutions for epilepsy and migraine through patient-physician connection

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Background and aims: Health solutions hold the promise to enhance personalized care, based on a deep understanding of the patient's health state and disease evolution. Efficiency depends on engagement of patients to ensure correct input, which tends to decline quickly over time due to app-fatigue. Good-in-class solutions have a retention rate of 30–40% after six months. Neuroventis provides interactive patient/healthcare professional (HCP) solutions for epilepsy (Helpilepsy) and headache (MigraineManager), allowing patients to opt-in on data sharing with their HCP, who has real-time access to a comprehensive dashboard summarizing events, adverse events, patient-reported outcomes and treatment.

Methods: We analysed anonymized data of Belgian patients having signed up to the epilepsy and migraine apps between 01-Jan-2019 and 31-Aug-2020. We evaluated the number of datapoints entered and retention rates after the first three and six months of usage for the standalone app users and for users having connected with their HCP.

Results: A total of 1,567 patients were enrolled, 560 for epilepsy and 1,007 for headache. Three and six month retention rate for standalone headache app users were 34% and 20% compared to 67% and 50% for connected patients. Similarly, for epilepsy, retention rates were 36% and 26% for standalone users compared to 76% and 64%. Data input by connected users was significantly higher both for quantity and detail.

Conclusion: Patients/HCP data sharing significantly increased retention rate, exceeding observed rates for similar standalone health apps. More research is required to understand the impact of data sharing and HCP involvement on efficacy of mHealth solutions.

Disclosure: Peter Dedeken has recieved consultancy fees from UCB Biopharma and Novartis. Jonathan Schreiber, Amandine Brewaeys and Olivia Langa are employees of Neuroventis. Jan Versijpt has recieved consultancy fees from various companies.

EPO-079

Subgroup analysis of galcanezumab treated patients meeting clinically meaningful response rates in the CONQUER trial

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Background and aims: Response rate, measured as the percentage of patients achieving a clinically meaningful reduction from baseline in the number of monthly migraine headache days, is a critical trial outcome to assess preventive treatment success. To understand how this translates into the corresponding number of monthly migraine headache days avoided in responders, we assessed the mean reduction in migraine headache days in galcanezumab treated patients who achieved a clinically meaningful response in CONQUER (NCT03559257).

Methods: CONQUER enrolled patients who previously failed 2–4 preventive categories for inadequate efficacy and/or safety/tolerability. A post-hoc analysis was conducted to estimate the mean change from baseline in the number of migraine headache days in galcanezumab responders at month 3, using a repeated measures analysis model for patients with episodic (EM), high frequency episodic (HFEM) or chronic migraine (CM) and ≥2 or ≥3 preventive category failures. Clinically meaningful response was defined as ≥50% decrease in migraine headache days from baseline in EM and HFEM; ≥30% and ≥50% decrease in CM.

Results: At Month 3, the percentages of galcanezumab responders ranged from 31.9% to 65.9% (Table 1). As expected, the changes in migraine headache days in responders (range from -6.57 (0.45) to -13.63 (0.86)) were higher than the changes observed for all galcanezumab patients (range from -2.90 (0.39) to -7.64 (1.30)) (Table 2).

	Episodic migraine	High-frequency episodic migraine	Chronic migraine
Galcanezumab patients with >=2 prior preventive medication category failures			
>=30% response (n/N; %)	NA	NA	51/88 (58.0%)
>=50% response (n/N; %)	55/136 (40.4%)	39/101 (38.6%)	32/88 (36.4%)
Galcanezumab patients with >=3 prior preventive medication category failures			
>=30% response (n/N; %)	NA	NA	27/41 (65.9%)
>=50% response (n/N; %)	18/55 (32.7%)	15/47 (31.9%)	19/41 (46.3%)

NA: Not analyzed in this patient population

Table 1: Percentages of galcanezumab patients with ≥30% or ≥50% reduction in migraine headache days at Month 3

	Episodic migraine	High-frequency episodic migraine	Chronic migraine
Galcanezumab patients with >=2 prior preventive medication category failures			
>=30% responders, mean (SE)	NA	NA	-11.30 (0.61)
>=50% responders, mean (SE)	-6.57 (0.45)	-7.20 (0.51)	-13.63 (0.86)
All galcanezumab patients	-2.90 (0.39)	-3.21 (0.46)	-6.57 (0.76)
Galcanezumab patients with >=3 prior preventive medication category failures			
>=30% responders, mean (SE)	NA	NA	-12.34 (0.99)
>=50% responders mean (SE)	-6.60 (0.79)	-7.37 (0.78)	-13.51 (1.27)
All galcanezumab patients	-3.42 (0.64)	-4.07 (0.64)	-7.64 (1.30)

NA: Not analyzed in this patient population; SE: standard error

Table 2: Mean change in monthly migraine headache days in galcanezumab responders (≥30% and/or ≥50%) and in the overall galcanezumab patient group

Conclusion: Galcanezumab responders experienced a reduction from baseline in migraine headache days almost twice as high as the full galcanezumab group. These results may help clinicians set realistic treatment expectations with patients initiating galcanezumab.
Disclosure: All the authors are employees of Eli Lilly and Company.

EPO-080

The potential to prevent unnecessary emergency department visits by timely diagnosis of migraine

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Background and aims: Headache is one of the most common causes for a presentation at the emergency department (ED). Patients are scared of a severe underlying disease and are looking for effective treatment. Migraine is the main aetiology of headache in the ED, and acute treatment would eventually prevent ED consultations, if the diagnosis of migraine had been given earlier. The aim of this study is to quantify the problem of missed diagnosis of migraine prior to ED visits.
Methods: Inclusion criterion for this single-centre prospective study was the presentation for acute headache at the ED. The treating physician assessed if patients had previous headache attacks fulfilling the ICHD-III criteria of migraine, and if they were given the diagnosis of migraine prior to the ED visit. Data was correlated with the discharge diagnosis.
Results: 100 patients were included of which 53 (53%) received the diagnosis of migraine at discharge. Of those, 20 never had migraine attacks before, and 16 already had the diagnosis of migraine. 33 (i.e. 62%) previously had fulfilled the criteria of migraine but had not been given the diagnosis.
Conclusion: About two thirds of patients presenting at the ED with migraine attacks could have been given the diagnosis of migraine earlier. Potentially, specific acute treatment might have prevented the presentation at the ED. This study demonstrates the need for better recognition of migraine by pre-hospital healthcare providers including pharmacists, primary care physicians, and neurologists.
Disclosure: This research has not been granted any commercial or institutional support.

EPO-081

Prevalence and Clinical Characteristics of Primary Headache among Medical Students in Khartoum State, Sudan Dec. 2020

G. Elfatih, E. Hasabo
Khartoum, Sudan

Background and aims: Headache is one of the most common complaints with significant prevalence among medical students; due to the physical and psychological stressors. It is classified into two types: primary (migraine, tension-type, and cluster) and secondary. This study aims to assess the prevalence of primary headache among medical students
Methods: This cross-sectional study was conducted, with randomized sampling ,among all classes of medical students of 10 universities in Khartoum state in December 2020. Students filled an online questionnaire derived from the Headache Intake Questionnaire and Headache screening questionnaire – a scoring system of eight points to screen for migraine and tension-type headache. Lifetime and last year headache prevalence which included demographic data, triggers and associated symptoms were among the measured variables.
Results: A total of 380 medical students participated in the study. The mean age was 21.17±2.00 years, and 109 (28.7%) of them were male (Table 1). The prevalence of headache was 289 (76%). Criteria for primary headache was fulfilled : tension-type headache=59 (20%) , migraine =219 (6.6%), while propable tension-type headache and propable migraine were 122 (42%) and 70 (24%), respectively.

Variables	N	N = 380[1]
Age, years	380	21.00 ± 2.00
Gender:	380	
Female		271 (71%)
Male		109 (29%)
University:	380	
Ahfad University		39 (10%)
AlNeelain University		44 (12%)
AlZaeim Alazhari University		39 (10%)
Bahri University		39 (10%)
El Razi University		34 (8.9%)
ElRibat University		44 (12%)
International University of Africa		30 (7.9%)
University of Khartoum		53 (14%)
National University		33 (8.7%)
Omdurman Islamic University		25 (6.6%)
Year of study :	380	
First		58 (15%)
Second		71 (19%)
Third		70 (18%)
Fourth		66 (17%)
Fifth		89 (23%)
Sixth		26 (6.8%)
Personal /Family monthly income:	354	
< 10,000 SDGs		37 (10%)
> 20,000 - 30,000 SDGs		73 (21%)
> 30,000 SDGs		163 (46%)
10,000 - 20,000 SDGs		81 (23%)
On average , how many hours of sleep do you get each night?	380	
< 5 hours		39 (10%)
> 8 hours		64 (17%)
5 - 8 hours		277 (73%)
Do you have problems falling/staying asleep?	377	147 (39%)
On average, how many meals do you eat each day?	377	
< 2 meals		118 (31%)
> 4 meals		6 (1.6%)
2 - 4 meals		253 (67%)
On average, how much caffeine cups do you consume daily?	380	
< 2 cups		155 (41%)
> 5 cups		10 (2.6%)
2 - 5 cups		71 (19%)
I don't drink caffeine		144 (38%)
Do you smoke cigarettes?	375	
Ex - smoker		5 (1.3%)
No		347 (93%)
Yes		23 (6.1%)
Do you use any illicit drugs?	378	
No		367 (97%)
Sometimes		5 (1.3%)
Yes		6 (1.6%)
How would you describe your health in general?	378	
Excellent		69 (18%)
Fair		56 (15%)
Good		243 (64%)
Poor		10 (2.6%)
In the past 12 months , have you ever had headache ?	380	289 (76%)

[1] Statistics presented: Mean ± Standard deviation; n (%)

Table 1: Baseline characteristics for all medical students.

Variables	N	Overall, N =
In your opinion , how bad are your headaches without medications?	289	
Mild		61 (21%
Moderate		162 (56%
Severe		64 (22%
Very severe/incapacitating		2 (0.7%)
Where do you feel the headache pain ?	289	
Both sides of the head		168 (58%
One side of the head		121 (42%
Where in your head do you usually feel the pain?(you can choose more than one)		
Front of the head	289	166 (57%
Back of the head	289	91 (31%
Right side of the head	289	176 (61%
Left side of the head	289	147 (51%
What word would you use to describe your headache pain?	289	
Burning or Stabbing		27 (9.3%
Pulsating or throbbing		134 (46%
Tight or pressing		128 (44%
Do any of the following triggers your headaches? (You can choose more than one)		
Hunger	289	124 (43%
Fatigue/exercise	289	147 (51%
Too little sleep	289	185 (64%
Too much sleep	289	67 (23%
Not enough caffeine	289	72 (25%
Too much caffeine	289	11 (3.8%
Stress	289	216 (75%
Coughing	289	38 (13%
Prolonged computer/phone use	289	117 (40%
Menstruation	289	62 (21%
Bright lights /Sun	289	143 (49%
Found sounds / noise	289	118 (41%
Weather/temperature changes	289	65 (22%
Specific foods	289	10 (3.5%
Specific odors	289	42 (15%
Drugs/medications	289	10 (3.5%
Do you experience any of the following "before" your headache begins? (You can choose more than one)		
Bright/multicolored/flashes of light	289	44 (15%
Zig-zag lines	289	20 (6.9%
Numbness/tingling	289	17 (5.9%
Visual disturbances	289	58 (20%
Paralysis	289	9 (3.1%)
Upset stomach/nausea	289	60 (21%
None	289	157 (54%
Do you experience any of the following "during" your headache? (You can choose more than one)		
Nausea/upset stomach	289	81 (28%
Vomiting	289	30 (10%
Dizziness/light headedness/vertigo	289	93 (32%
Numbness/tingling	289	12 (4.2%
Eye tears	289	90 (31%
Runny/stuffy nose	289	28 (9.7%
Mood changes/irritability	289	150 (52%
Difficulty concentrating	289	176 (61%
Bright lights bother you	289	149 (52%
Loud sounds bother you	289	131 (45%
What makes you comfortable during a headache? (You can choose more than one)		
Lying down/sleeping	289	228 (79%
Keeping physically active	289	14 (4.8%
Massage your head	289	130 (45%
Cold pack on head/neck	289	25 (8.7%
Hot pack on head/neck	289	7 (2.4%)
Being in a dark/quiet room	289	171 (59%
Tying something around your head	289	61 (21%
Having a cup of tea/coffee	289	93 (32%

Table 2: Characteristics of headache among medical students.

Conclusion: The prevalence of primary headche was high among medical students. Few students were suffering from migraine while on the other hand , prevalence of tension-type headache was higher among medical students. Special care is needed for the medical students who experienced a decrease in ability to function as a consequence of their headaches.

Disclosure: Nothing to disclose.

EPO-082

Neuropathic pain mechanisms in painful polyneuropathies. Learnings from type 2 diabetes and TTR-FAP.

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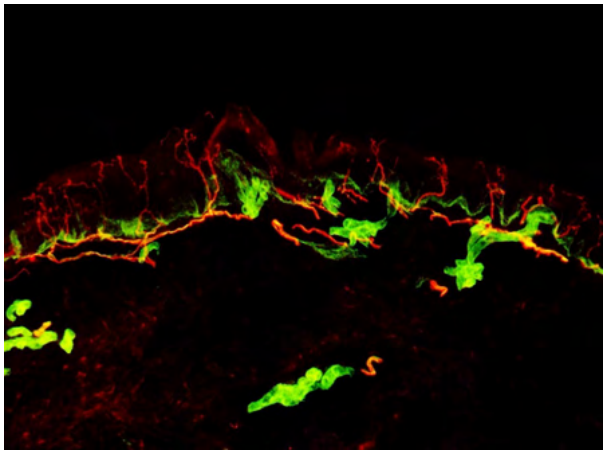
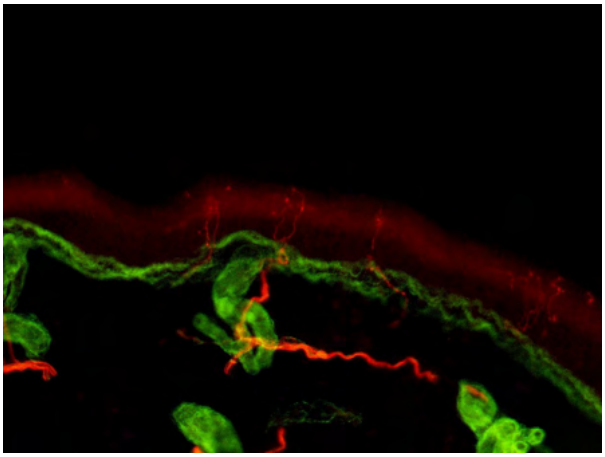
Background and aims: Patients with polyneuropathy frequently complain of neuropathic pain. Though small-fiber damage is traditionally considered the hallmark of painful polyneuropathies, it is still unclear how neuropathic pain is associated with detectable small fiber impairment. Our prospective study aims at characterizing distinct small-fiber abnormalities in two representative groups of painful polyneuropathies, diabetic polyneuropathy and transthyretin familial amyloid polyneuropathy (TTR-FAP), by QST sensory profiling and skin biopsy.

Methods: We enrolled 31 patients with type 2 diabetes-related polyneuropathy and 20 TTR-FAP patients. Each individual underwent clinical examination, neuropathic pain questionnaires, nerve conduction study, QST from foot and hand, skin biopsy at distal calf. Each patient was sorted to a specific QST sensory profile through a deterministic algorithm. Intraepidermal nerve fiber density (IENFD) was assessed by immunostaining of the pan-neuronal marker PGP9.5 and the axonal regeneration marker GAP43 at skin biopsy.

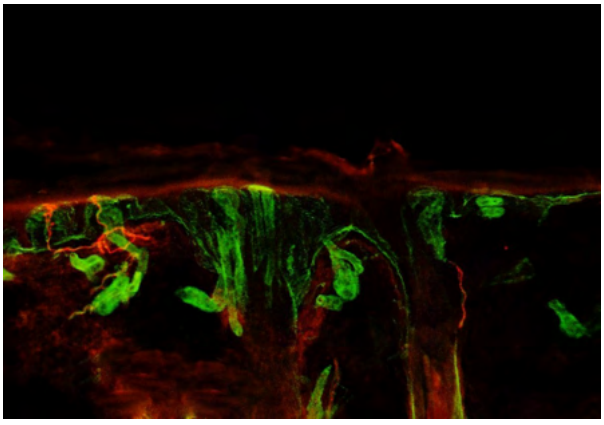
Results: 67% of diabetic and 60% of TTR-FAP patients suffered from neuropathic pain. Patients with painful diabetic polyneuropathy and painful TTR-FAP showed similar neuropathic pain characteristics and similar QST abnormalities, Patients with painful TTR-FAP had a lower PGP9.5 IENFD and lower regeneration rates as assessed by GAP43 than patients with painful diabetic polyneuropathy.



Skin biopsy image taken with fluorescence microscope and using immunostaining with protein gene product 9.5 (red) and collagen (green). Healthy control.



Diabetic patient.



TTR-FAP patient

Conclusion: Our findings suggest that in patients with different types of painful polyneuropathy similar symptoms and signs might be mediated by different small-fiber abnormalities. Patients with painful diabetic polyneuropathy and painful TTR-FAP have similar combinations of sensory symptoms, however patients with painful TTR-FAP have lower IENFD and a lower nerve regeneration.

Disclosure: Nothing to disclose.

MS and related disorders 1

EPO-083

Third nerve palsy in multiple sclerosis: case report and literature review

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Background and aims: Multiple sclerosis (MS) is a chronic, autoimmune, demyelinating disease of the central nervous system. Although brainstem involvement is common at MS onset and during the course of the disease, isolated cranial nerve involvement is rare in MS patients and especially 3rd nerve palsy. In this study we present a rare case of third cranial nerve palsy triggered by an acute relapse of multiple sclerosis and correlate our findings with a brief review of literature.
Methods: N/A
Results: A 30-year old woman followed up for relapsing-remitting multiple sclerosis. She was treated with Interferon-beta. She was admitted to our department 10 days after the onset of binocular horizontal diplopia and right upper eyelid ptosis. On examination, her visual acuity was 10/10 in both eyes. She demonstrated 1mm of anisocoria, with the right pupil larger than the left. There was 1mm of right upper eyelid ptosis. There were adduction deficits on the right. Brain MRI revealed bilateral periventricular white matter hyperintensities and spinal MRI showed two hyperintense lesions at the D11-D12 vertebral levels. The patient was treated with five days of IV methylprednisolone with a good outcome.
Conclusion: Despite the rarity of CN III palsy as a clinical manifestation of MS relapse, demyelinating disease should remain on one's differential diagnosis, particularly in young patients without typical microvascular risk factors.
Disclosure: Nothing to disclose.

EPO-084

Is SARS-CoV-2 important for multiple sclerosis?

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Background and aims: Multiple sclerosis (MS) is an autoimmune disease of the central nervous system (CNS). COVID-19 pandemic is caused by SARS-CoV-2. The huge amount of scientific evidence tells us that SARS-CoV-2 is both neurotropic and neurovirulent. The virus enters the CNS shortly after infection and is found in cerebrospinal fluid and brain tissue, what can lead to an inflammatory cascade in the nervous system and progressive demyelination.
Methods: We studied 218 patients (mean age 38±7.6 years, M:F=83:135) with MS (relapsing types) who are under long-term ambulatory observation and have prophylactic therapy. 17 of them were ill with COVID-19 (M:F=4:13). All patients were undergone neurological and MRI examination after the COVID-19.
Results: During six months prospective study we haven't identified any cases of changes in the type of course (according to clinical and radiological signs) after the COVID-19 among these patients. One of the patients suffered from COVID-19 in severe form (more than 75% of the lung tissue was radiologically affected) and was on oxygen support at the intensive care department. After recovery, the patient underwent MRI of the brain with contrast, which showed no signs of MS activity or progression and clinical signs of disease activity also weren't detected for six months from the undergone COVID-19.
Conclusion: Thus, the opinion about the negative impact of SARS-CoV-2 on the course of MS is premature, which requires further study and observation of these patients.
Disclosure: Nothing to disclose.

EPO-085

Severe Susac syndrome during pregnancy requiring ICU admission: a challenging clinical case

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[1] Coimbra, Portugal, [2] Neurology, Coimbra, Portugal, [3] Ophtalmology, Coimbra, Portugal, [4] 1st Department of Neurology, Coimbra, Portugal

Background and aims: Susac syndrome (SS) is a rare vasculitic disorder, characterized by encephalopathy, visual deficits and sensorineural hearing impairment.
Methods: N/A
Results: A 24-year-old woman, pregnant (24-week), with multiple admissions in the previous month for headache and blurred vision presented to the emergency room with complaints of right lower limb weakness. Physical examination revealed confusion, inappropriate behaviour and non-consistent weakness of right limbs. Cranial computed tomography was normal. Psychosomatic disorder was considered and patient was admitted in the psychiatry ward and started on antidepressants/neuroleptics. During her stay, she developed fever, generalized muscular rigidity and dystonic posture. Neuroleptic malignant syndrome was considered and she was started on dantrolene. Cerebrospinal fluid examination revealed elevated proteinorrachia and leukorrhachia. Brain magnetic resonance imaging revealed multiple lesions in different temporal phases, namely in corpus callosum and internal capsule localization. Infectious encephalitis was initially considered and she was started on antiviral/antibiotic therapy. At 28-week pregnant, she was admitted in the intensive care unit because of consciousness depression. Central nervous system vasculitis was considered and patient was started on high-dose methylprednisolone and immunoglobulin G. At 32-week pregnant, a planned caesarean was performed. A SS was presumed and rituximab was started. The patient slowly improved and fluorescein angiography and audiogram were performed, revealing left occlusive vasculitis and bilateral sensorineural deafness, respectively.
Conclusion: This case of a severe SS in a pregnant woman emphasises the importance of considering this condition in the differential diagnosis of neuro-psychiatric disorders presenting during pregnancy so that early identification and prompt start of treatment is provided.
Disclosure: No disclosures.

EPO-086

A Computational Model with Theoretical Nuclear Physics Methods for Lesion Dynamics in Multiple Sclerosis of the Brain

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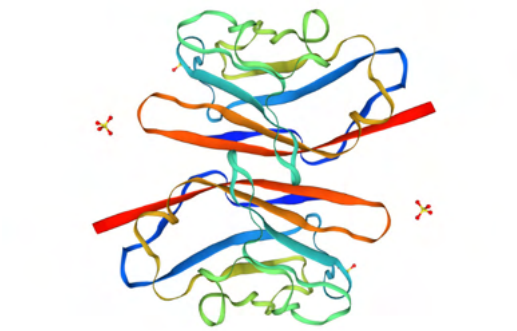
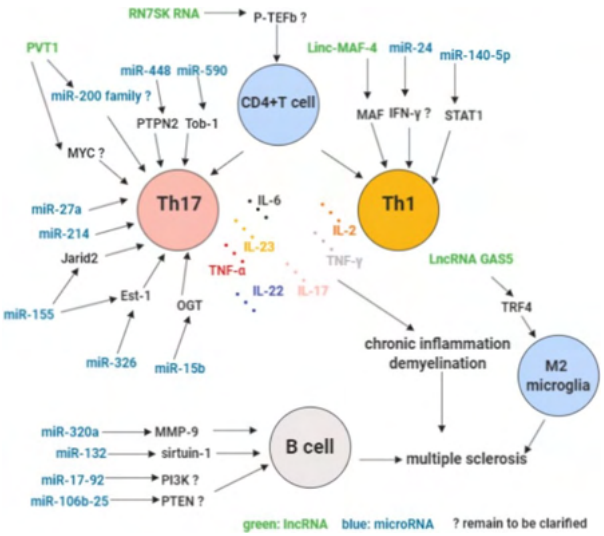
Background and aims: The presence of demyelination plaques in various parts of the central nervous system and formation of glial scars are characteristic of the pathophysiology of multiple sclerosis (MS). This study aims to develop a computational model with theoretical nuclear physics methods for lesion dynamics in multiple sclerosis of the brain.
Methods: The model was elaborated based on computational simulations that analyzed (a) the immunological mechanisms in MS; (b) the putative mechanisms of action of histone-modifying enzyme inhibitors; (c) the mechanisms of noncoding (nc) RNAs in MS. An undirected, fixed radius random graph G(n, r), with n nodes (vertices) and radius of connectivity, r, is constructed to represent the central nervous system in this 2D network model; fixed radius implies that nodes are connected only if they are within a distance of r. The pathological and regeneration processes are driven by probabilistic events wherein each edge in the affected region, in each time unit, has a certain probability pd (pr) of getting damaged (regenerated). The model, computational simulations and analyzes of this scientific work were elaborated with the use of software: ACD/ChemSketch, Swiss-PdbViewer, ABCpred, BepiPred-2.0, DEseq, GOseq, BiNGO, AxonDeepSeg, Computer-assisted Evaluation of Myelin formation (CEM), PyMol, ICM-Browser, Visual Molecular Dynamics (VMD), C-ImmSim, Simmune and ChemDraw.

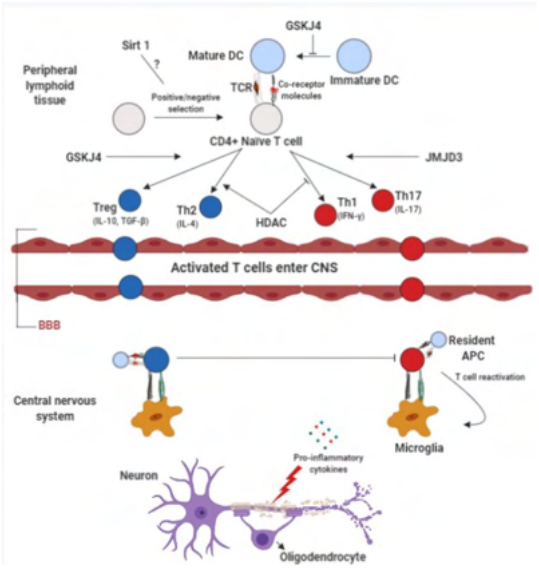


The crystal structure of an autoantigen in multiple sclerosis (X-ray Diffraction, 1.80)

Results: This model demonstrates the cascade of events possibly underlying autoimmunity-related demyelination in MS, putative mechanisms of action of histone-modifying enzyme inhibitors and mechanisms of ncRNAs in MS.



Mechanisms of ncRNAs in MS



Immune mechanism in MS

Conclusion: Investigations into the disruption of the homeostatic balance of the immune system should help guide future research into MS therapeutics.
Disclosure: Nothing to disclose.

EPO-087

Rituximab in multiple sclerosis: a tertiary hospital experience

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Background and aims: B-lymphocytes play an important role in the pathophysiology of MS. As with other anti-CD20-antibodies, there is evidence that Rituximab may be effective and safe in this disease.
Methods: Retrospective study in MS patients treated with Rituximab between 2017–2021. Demographic, clinical, radiologic and laboratory variables were analyzed.
Results: 45 patients were included (60% males, mean age 48.3±8; 84.4% presented SPMS; median baseline EDSS 6.0, IQR 4-6.5; mean follow-up 22.69±8.75 months). After one year of treatment, there was a significant reduction of relapses (ARR 0.51 vs 0.1, p=0.002), new/enlarged T2 lesion (60% vs 10%, p<0.001) or gadolinium-enhancing lesions (40% vs 0%, p<0.001) on MRI. EDSS, T25FWT, 9HPT or SDMT did not significally change. 33.3% presented confirmed disability progression (CDP). 56.4% achieved NEDA-3. Retreatment was guided by B-lymphocytes count. Mean B-cells count was 285.7, 1.553, 4.456, 54.35, 10.47 at baseline, 3, 6, 9 and 12 months, respectively. Mean time to retreatment was 9.05±3.14 months. Lipidospecific IgM-OCB were associated with CDP (adjusted OR 6.33, p=0.047). At first dose, 31.1% presented an infusion reaction, with fewer cases with retreatment. 28.8% presented infections of any kind, including three cases of Covid19 (only one case of severe infection was reported). No cases of hypogammaglobulinemia were reported.
Conclusion: B-lymphocytes count guiding retreatment with Rituximab among patients with MS may favor a good safety profile, while being effective in reducing inflammatory activity. CDP was associated with lipidospecific IgM-OCB.
Disclosure: There are no conflicts of interest to disclose.

EPO-088

Interleukin 32 Gene Promoter Polymorphism and Serum levels of Interleukin 32 in Multiple Sclerosis

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Background and aims: Multiple sclerosis is a chronic inflammatory disorder of unknown etiology. Various genetic and acquired risk factors exist, however. The present study was done to determine whether the IL-32 gene promoter polymorphism is a genetic risk factor for the development of multiple sclerosis and whether any relationship exists between serum IL-32 levels and multiple sclerosis.
Methods: 48 relapsing remitting multiple sclerosis patients and 60 healthy controls were compared for IL-32 gene promoter polymorphism and IL-32 levels.
Results: There was no significant difference in genotype CT between the MS patients and healthy controls (p= 0.130). There were a significant difference in genotype (CC) frequencies among MS patients and healthy controls (p=0.039). The difference in C allele frequency was also statistically significant between the two study groups (p=0.01). Multivariate regression analysis revealed that the CC genotype might impact the risk of disease susceptibility up to 3.71 times and the presence of the C allele might increase the risk of susceptibility to multiple sclerosis by 2.26 fold. The serum IL-32 levels were not statistically different from multiple sclerosis patients and healthy controls and between wild and mutant genotypes.
Conclusion: This study shows IL-32 gene promoter polymorphism as a genetic risk factor for multiple sclerosis, particularly in women.
Disclosure: Nothing to disclose.

EPO-089

Influence of autologous mesenchymal stem cell transplantation on the disability outcomes in patients with MS

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[1] Department of Neurology & Neurosurgery, Minsk, Belarus, [2] Minsk, Belarus

Background and aims: Mesenchymal stem cells (MSC) have a neuroprotective effect. MSC is able to express neuroregulatory molecules. MSC-transplantation allows achieving immunomodulation. Current research purpose was to explore influence of the autologous MSC transplantation (aMSCT) on course of multiple sclerosis (MS).
Methods: This study was recruiting 20 patients with Relapsing-Remitting Multiple Sclerosis (RRMS). Diagnosis was verified according to McDonald criteria e.a. (2017). Main group consisted of 10 patients under aMSCT. Comparison group consisted of 10 patients under symptomatic therapy. Average amount of transplanted MSC was 1.64±0.71 million cells per kilogram. Both groups were comparable on clinical and demographic characteristics, neurological conditions e.a
Results: Neurological evaluation on EDSS before aMSCT and after 26.8±5.8 months did not show statistically significant increasing of neurological deficiency in main group (Wilcoxon=1.47, p=0.14). We observed reliable increasing of neurological deficiency (Wilcoxon=2.67, p=0.008) in comparison group after 21.8±4.0 months. Average EDSS-score in main group within two years observation was reliably lower than in comparison group (Fisher exact p=0.043, one-tailed). Relative risk of increasing neurological deficiency above 0,5 point on EDSS-score in control group was 1.83 times higher than in main group (95% confidence interval 0.92-3.82). The number of active demyelination lesions according to MRI results was significantly less (2=7.2, p=0.0073) among patients with MS under aTMSC in compare with comparison group.
Conclusion: Neurological evaluation patients with RRMS show neurological deficiency stabilization after autologous MSC-transplantation within two years observation.
Disclosure: Nothing to disclose.

EPO-090

High-dose chemotherapy with support for autologous hematopoietic stem cell transplantation in multiple sclerosis

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[1] *Department of Neurology & Neurosurgery, Minsk, Belarus,* [2] *Minsk, Belarus*

Background and aims: High-dose polychemotherapy (HPCT) followed by autologous hematopoietic stem cell transplantation (HSCT) is the eradication of the pool of autoreactive immune cells by intensive immunosuppression with further complete immune reconstitution.
Methods: The main group (MG) included 21 patients with clinically defined Multiple Sclerosis (MS) under HPCT+aHSCT. Diagnosis was verified according to McDonald criteria e.a. (2017). The comparison group (CG) included 21 patients with MS. HPCT was performed according to two protocols: antithymocyte immunoglobulin (ATG)+cyclophosphamide (CP)+methylprednisolone (MP) – 10 patients and BEAM-CSA protocol – 11 patients.
Results: The most frequent complication from various modes of HPCT were hematological toxicity (100%). Patients from MG showed progression of neurological symptoms (2=28.26; $p<0.001$) within two years prior to HPCT+aHSCT. There was no statistically significant increase of disability outcomes on the EDSS during the observation of patients in the post-transplant period within 41.8 (29.0±67.2) months. The analysis of event-free survival cases showed better results among patients under aHSCT in contrast with CG ($p<0.05$); Gehan-Wilcoxon test: statistical criterion=4.53, p=0.00001; Cox F-test: F (18; 38) =6.996, p=0.00000). There were no statistically significant differences in the disability outcomes after aHSCT between ATG+CP+MP and BEAM-CSA ($p<0.05$). The observation during three years showed 100% cases of MRI results stabilization in MG and 4.8% ones in the CG.
Conclusion: Application HPCT+aHSCT allowed reducing the rank of disability and increasing the duration of the period without exacerbations. ATG+CP+MP and BEAM-CSA are comparable in efficacy and tolerability.
Disclosure: Nothing to disclose.

EPO-091

Cost-effectiveness analysis of multiple sclerosis cell therapy

A. Fedulau [1], A. Barisau [2], R. Aghayev [2]
[1] *Department of Neurology & Neurosurgery, Minsk, Belarus,* [2] *Minsk, Belarus*

Background and aims: Cost-Effectiveness Analysis (CEA) estimates the costs and health gains of alternative interventions for patients with Multiple Sclerosis (MS).
Methods: This study was recruiting 121 patients with clinically defined MS. The main group included 67 patients who underwent cell therapy: high-dose polychemotherapy (HPCT) followed by autologous hematopoietic stem cell transplantation (HSCT) (n=24), HPCT and o-transplantation HSCT and autologous mesenchymal stem cells (aMSC) (n=24), aMSC transplantation (aMSCT) (n=19). Comparison group consisted of 54 patients under symptomatic therapy. CEA ratio was assessed for various options of cell therapy and symptomatic therapy for patients with MS per 100 patients. CEA ratio was calculated using the following formula: CEA = (costs of symptomatic treatment×100) - (costs of symptomatic treatment×100)/ 1-year relapse-free survival after cell therapy (%) - one-year relapse-free survival when using symptomatic therapy (%).
Results: 1-year disease-free survival rate after cell therapy equal 100%. One-year disease-free survival rate in the comparison group equal 38%. CEA (the price per Life Years Saved) is 1712USD – aMSCT, 9792USD – HPCT+HSCT, 15183USD – HPCT+HSCT+aMSCT. HPCT+HSCT and HPCT+HSCT+aMSCT allowed preventing of relapses / progression of disease during three years of patient observation. Consequently, the cost of saved life over a 3-year after HPCT+HSCT equals 3264USD, HPCT+HSCT+aMSCT – 5061USD.
Conclusion: According to most healthcare professionals, an acceptable cost is up to 30,000 USD per year for every saved life. In view of the above, the use of cell therapy for MS is justified in terms of the CEA.
Disclosure: Nothing to disclose.

EPO-092

Immunization status of multiple sclerosis patients in Latvia

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Background and aims: Multiple sclerosis (MS) is the most common immune-mediated inflammatory demyelinating disease of the CNS. Patients are often concerned about the safety of immunization – its effect on MS, interactions with treatments and possible adverse effects. This study aimed to compare the immunization status of MS patients and general population and determine factors affecting patients' choice to vaccinate.
Methods: A cross-sectional study was conducted in July-December 2020 among two populations: MS patients at Riga East University Hospital's Outpatient clinic and online control group (CG). A questionnaire was designed based on adults' vaccination recommendations in Latvia. Data was analyzed using SPSS-26 software.
Results: The study included 65 MS patients and 6,370 participants in the CG. The average age of MS patients was 41.5 (SD 12.8) and 42.6 (SD 12.45) in the CG. Highest immunization status was diphtheria (81.5%) in MS patients and tetanus (73.4%) in CG. Lowest immunization status for both groups was Meningococcal infection: 1.5% in MS patients and 0.4% in CG. MS patients had lower immunization levels than CG for seven of 21 vaccines, of which poliomyelitis and tick-born encephalitis were statistically significant ($p<0.05$). When asked to consider the validity of statements regarding immunization safety, 87.7% (n=57) of MS patients believe the cause of MS is vaccine-related while 63.1% (n=41) agree vaccines exacerbate MS.
Conclusion: MS patients had lower immunization status levels for certain vaccines, however only two were statistically significant. Nearly 90% of interviewed MS patients believe the cause of MS is vaccine-related and more than half believe it causes MS exacerbation.
Disclosure: Nothing to disclose.

EPO-093

Prevalence of sleep disturbances in relapsing-remitting multiple sclerosis: single-center prospective cohort trial

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Background and aims: Sleep disturbances can have a significant impact on daily activities. The incidence of sleep disorders in the MS patient population is still unclear.
Methods: Aim: To define the frequency and severity of sleep disturbances (SD) and daily activity in relapsing-remitting MS cohort on first disease modifying drugs (DMD) **Methods:** Clinical evaluation (EDSS, relapses), MRI (T2&T1), Pittsburgh Sleep Quality Index (PSQI), Quality of Life (SF-36). Statistical analysis (nonparametric) – Wilcoxon test, Sign test, Spearman test. Inclusion criteria: 1) relapsing-remitting MS, 2) DMD therapy for al list six month. Exclusion criteria: 1) progressive MS, 2) severe comorbidity. Study design: One hundred and seventy-two patients (49 males), relapsing-remitting MS, age – 43.6 years [Q1:Q3; 34:53], duration of disease – 105.4 months [51.4:199.4], EDSS – 2.0 [1.5:3.5], DMT (GA–47, pegIFN–33, IFNb1b–46, IFNb1a–25, teriflunomide–16, fingolimod–5) who met criteria.
Results: 40 (23%) have mild SD and 10 (6%) have moderate. 23.5% with EDSS rate3 and 42.9% with EDSS rate>3 have altered sleep and daily sleepness. No difference in relapse rate and MRI activity between groups. More severe SD have patients with higher EDSS rate ($p<0.001$). Patient with more severe disability have higher sleep latency ($p=0.003$) and daily sleepiness ($p=0.003$). Pattern of sleep problems depends on disability level. Patient using teriflunomide have more severe daily sleepiness ($p=0.03$). Severity of SD have strong correlation with SF-36 ($p<0.001$).
Conclusion: Sleep disturbances is frequent problem in MS patients' population. Problem with night sleep and daily activity significantly decrease the quality of life. Teriflunomide potentially has more behavioral toxicity between another 1st-line DMD.
Disclosure: Nothing to disclose.

EPO-094

Potential efficacy of SSRI in relapsing-remitting multiple sclerosis patients with suboptimal response

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Background and aims: Suboptimal response for 1st line treatment of MS is one of the main challenges for real clinical practice. Presence of subthreshold activity suggests the possibility of switching to the 2nd line of therapy, however, this is not always possible due to various reasons.
Methods: Aim: To define the possibility of using duloxetine or fluoxetine for patients with suboptimal response on 1st-line injectable therapy Methods: Clinical evaluation (EDSS, relapses), depression (Beck), MRI (T2&T1). Statistical analysis (nonparametric). Inclusion criteria: 1) relapsing-remitting MS, 2) IFN or GA during last 12 months, 3) suboptimal response for therapy defined by modified Rio Score, 4) mild or moderate depression. Study design: visit 1 – baseline, starting SSRI (duloxetine or fluoxetine); visit 2 – 1 year on SSRI + previous DMT or DMT alone.
Results: 70 patients (56 females), relapsing-remitting MS, age – 35.2 years [Q1:Q3; 28:42], duration of disease – 4.2 years [2:10], EDSS at visit 0–3.0 [2.4:3.6], DMT (GA–20, IFNb1b–30, IFNb1a–20) who met criteria at visit 1. Compatible control group – 24 patients (17 females). After one year of combined therapy (DMT+SSRI) relapse rate significantly decreased – 0.2 ($p<0.001$), no significant increase of EDSS level – minus 0.36 points. MRI activity also significantly decrease: numbers of new or newly enlarging T2 lesions were significantly reduced compared with the previous year: T2 lesion load increase only by 0.4 [95%CI=0.3-0.5] ($p<0.001$).
Conclusion: Adding SSRI to standard first line DMT for patients with suboptimal response could improve the response to the main DMT without switching to 2nd line.
Disclosure: Nothing to disclose.

EPO-095

Epidemiological and clinical characterisation of Belgian patients with Susac syndrome: preliminary results

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Background and aims: Susac syndrome (SS) is a rare autoimmune endotheliopathy with involvement of the microvessels of brain, inner ear and retina, leading to the characteristic clinical triad of encephalopathy, sensorineural hearing loss and visual disturbance due to branch retinal artery occlusions. While no randomized controlled trials are available to guide treatment, current guidelines recommend early aggressive immunosuppressive therapy to prevent long-term sequelae.
Methods: All neurology departments in Belgium were addressed to report patients with a diagnosis of SS and provide demographic and clinical and results of ancillary investigations.
Results: To date, we identified 31 patients with SS treated at Belgian hospitals. Detailed information on 10 of them is presented here; data on the additional 21 patients will be presented at the congress. Nine patients were female and mean age at diagnosis was 31 years (standard deviation six years 11 months). Four patients presented with the characteristic clinical triad and two more developed the triad further along their disease course. Nine patients had abnormalities on brain MRI, eight of which had typical callosal lesions. All patients had signs of ocular inflammation on fluorescein angiography. Seven patients had abnormal audiograms. Treatment consisted of one or more of the following: corticosteroids (all patients), acetylsalicylic acid (7), rituximab (6), intravenous immunoglobulins (5), mycophenolate mofetil (4), azathioprine (3) and/or cyclophosphamide (2). Six patients are currently in remission, of which four have some sequelae.
Conclusion: We provide for the first time epidemiological and clinical data on a multicentric cohort of Belgian Susac patients.
Disclosure: The authors have no disclosures.

EPO-096

Pain in patients with multiple sclerosis

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Background and aims: Pain can have a negative impact on daily living in multiple sclerosis (MS) patients. The estimated prevalence of pain in MS ranges widely from 26 to 86%.

Objective: To assess prevalence of different types of pain, their relationship to depression, anxiety, sleep disorders, quality of life in MS patients.

Methods: 203 MS patients (57 males), average age 42.8, EDSS-3.7, 189-relapsing-remitting, 14-secondary progressive MS. Structured face-face interviews focused on MS-related types of pain (A.Truini, 2012), experienced in the month preceding the assessment, clinical evaluation, Beck Depression Inventory (BDI), State-Trait Anxiety Inventory (STAI), Pittsburgh Sleep Quality Index (PSQI), Quality of Life (SF-36).

Results: 147 (72,4%) patients reported at least 1 type of pain, more frequent in females than males (p=0,001). The ratio of different types: 42, 4% neck or low back pain, 13,3% painful tonic spasms, 12,3% central neuropathic pain (CNP), 11,8% Lhermitte's sign, 9,4% migraine, 5,4% spasticity pain, 1,0 % trigeminal neuralgia; 34,5% patients reported 2 and 11,3% – three and more concurrent pain locations. Pain limited daily activities in 61,2% patients. Depression or anxiety occurred in all patients with three or more concurrent pain locations. Neck or low back pain prevalence was associated with MS duration and higher EDSS rate ($p<0.001$). CNP prevalence and severity had strong correlations with sleep disorders and lower SF-36 Physical Health Score ($p<0.001$); 40,0% patients with CNP didn't get an appropriate therapy.

Conclusion: Pain is a major burden for MS patients. Identification of various types of pain will allow targeted treatment and improve clinical practice.

Disclosure: Nothing to disclose.

Muscle and neuromuscular junction disease 1

EPO-097

Respiratory predominant case of Congenital Myasthenia associated with a new variant of the AGRN gene

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Background and aims: Agrin (AGRN) mutations cause congenital myasthenic syndromes (CMS). Facial diparesis, ptosis, distal-predominant limb weakness and difficulty running are the most frequent features, with some patients requiring respiratory support later in life. Response to salbutamol and no benefit with anti-AChE drugs is well documented.
Methods: A 27 years old female was referenced to the neuromuscular clinics after two admissions due to acute respiratory failure and arreflexic tetraparesis, maintaining the need for nocturnal non-invasive ventilation since then. During childhood she was never able to run like her peers. The examination shows an elongated face, ogival palate, nasal voice, mild hypotonic tetraparesis, joint laxity and a myopathic gait. Her CK and thigh and brain MRI were unremarkable. EMG with repetitive nerve stimulation (RNS), was normal. A congenital myopathy was suspected, but muscle biopsy (deltoid) only showed occasional atrophic fibers. She repeated RNS which showed a post-exercise exhaustion at anconeus muscle.
Results: Direct sequencing revealed a pathogenic mutation of the DOK7 gene in heterozygosity and a variant at the AGR gene (c.5315_5317del) in homozygosity, causing a deletion of a serine at position 1,772 on the laminin G-like domain 2, a very close site to known pathogenic mutations. Segregation studies are now pending. Her strength improved markedly after salbutamol introduction but still complains of dyspnea.
Conclusion: This case reveals a new variant, with a phenotype compatible with an AGRN mutation with a predominant respiratory phenotype and no ptosis. A high level of suspicion for CMS must be kept in cases compatible with congenital myopathy with normal muscle biopsy.
Disclosure: The authors did not received any support from the pharmaceutical industry. The patient has given consent.

EPO-098

ETFDH mutations as a major cause of secondary carnitine deficiency

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Background and aims: Lipid storage myopathies (LSM) are characterized by accumulation of lipid droplets and may present with myalgia, severe systemic manifestations weakness or myoglobinuria. We present two siblings with these clinical features, LSM, were two heterozygous ETF-dehydrogenase mutations were found, one novel.
Methods: Carnitine in blood and muscle were studied by a radioactive assay. ETFDH mutations were studied in the second patient.

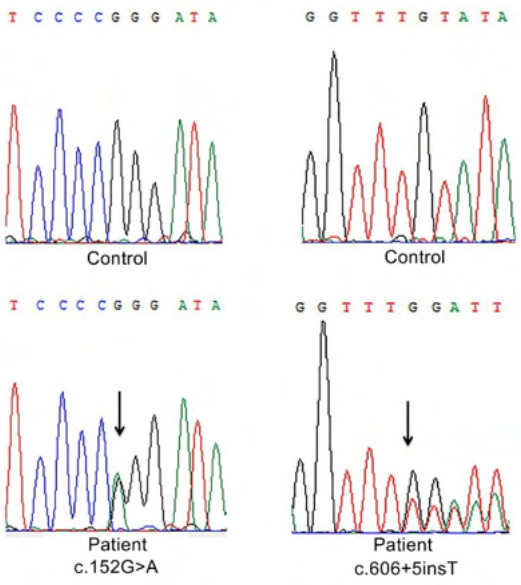

Figure 2. Genetic analysis of ETFDH gene in MADD patient
Electropherograms showed two mutations identified in exon 2 and 5. The first one is a missense mutation, c.152G>A (p.R51Q); the second is a novel splite-site mutation (c.606+5insT) that determines the production of a truncated protein.

Electropherogram shows two heterozygous ETFdehydrogenase mutations, one novel in exon 2 and 5

Results: Two siblings were referred to our center for a LSM.The first one was a 16 year old woman, that had profound weakness during her 1st pregnancy,and was found affected by carnitine deficiency, partially recovered with carnitine treatment and died from sepsis. The older brother 33-year old came after a myoglobinuric episode ,was found affected by exercise intolerance, treated with carnitine and riboflavin and fully recovered.
Conclusion: Although with heterogeneos clinical presentation and outcome this couple of siblings illustrates the importance of molecularly diagnosing and treating LSM.ETDH mutations might cause multiple
CoA-dehydrogenase deficiency with secondary carnitine depletion.
Disclosure: AFM grant 22392

EPO-099

Long-term outcome in patients with myasthenia gravis

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Background and aims: Even treated, myasthenia gravis (MG) continues to represent a significant burden and might continuously affect patients' quality of life (QoL). The aim of our longitudinal study was to analyze QoL in a large cohort of MG patients after a ten-year follow-up period.

Methods: This study comprised 78 MG patients (60% females, 50±16 years old at baseline, 70% AchR positive) who were retested after ten years. Disease severity was evaluated by MGFA classification. QoL was assessed using SF-36 questionnaire and Myasthenia Gravis-specific Questionnaire (MGQ). Hamilton rating scales for depression and anxiety (HDRS and HARS), the Multidimensional Scale of Perceived Social Support (MSPSS) and the Acceptance of Illness Scale (AIS) were also used.

Results: Similar percentage of patients was in remission at both time points. All patients were treated at baseline, while 32% were treatment-free at follow-up. SF-36, MGQ, MSPSS and AIS scores were similar at baseline and retest, while HDRS and HARS scores worsened during time ($p<0.05$). Significant predictors of worse SF-36 score at retest were depression (=-0.453, $p<0.01$), poor disease acceptance (=-0.438, $p<0.01$) and older age (=-0.297, $p<0.01$). Significant predictors of worse MGQ score were poor disease acceptance (=-0.402, $p<0.01$), retirement (=-0.363, $p<0.01$), lower education (=0.250, $p<0.01$), and depression (=-0.185, $p<0.05$).

Conclusion: Although after ten years majority of MG patients were in remission, their QoL was still reduced. Neurologists should be aware that poor QoL may persist even if MG is well treated.

Disclosure: The authors declare that they have no conflict of interest.

EPO-100

Symptomatic female carrier of familial dystrophinopathy

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Background and aims: Duchenne (DMD) and Becker muscular dystrophy are X-linked recessive diseases caused by the dystrophin gene mutations. Males are affected whereas females are usually asymptomatic carriers. About 8% of female carriers have muscle weakness and/or cardiomyopathy. Signs and symptoms of muscle weakness may differ from those usually seen in affected man.

Methods: Clinical Case

Results: A 37-year-old female with no relevant clinical history was referred to a neuromuscular disease appointment with suspected inflammatory myopathy. She presented with unilateral pain and atrophy of posterior right leg muscles and elevation of creatine kinase levels (970UI/L) since her thirties. She had a family history of DMD in two brothers, two maternal uncles and a cousin. Neuromuscular examination showed atrophy of the right internal gastrocnemius muscle and difficulty on toe-walking without weakness in other segments. Motor and sensory nerve conduction studies were normal and needle electromyography revealed a myopathic pattern with increased resistance to needle insertion in the atrophied muscle. CT scan showed atrophy and adipose infiltration of right internal gastrocnemius muscle, reduction of right external gastrocnemius muscle volume and adipose infiltration of internal left gastrocnemius muscle without atrophy. Genetic testing confirmed that she was a dystrophinopathy carrier. Cardiac studies were unremarkable.

Conclusion: Identification of female dystrophinopathy carriers is extremely important for a correct follow-up (genetic counselling and cardiac evaluation). In this case less suggestive manifestations of a dystrophinopathy with distal and asymmetric weakness, with associated pain, motivated an initial search for other diagnoses despite the positive family history.

Disclosure: No disclosures.

EPO-101

Acute rhabdomyolysis associated to treatment with Sorafenib

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Background and aims: Tyr-kinase inhibitor sorafenib has proven efficacy in patients with advanced hepatocellular carcinoma. Previous reports have related sorafenib with isolated cases of myositis or rabdomiolisis.
Methods: Case report.
Results: A 59 years old with previous history of cyrrhosis secondary to alcohol consumption and complicated with hepatocellular carcinoma initiated sorafenib after evidence of tumoral progression. He soon showed adverse effects, as diarrhea or asthenia. After 48 hours, he started progressive weakness of proximal predominance and speech disturbances, and after five days he precised a wheelchair. Neurological examination revealed proximal weakness 4/5 in arms and 1/5 en both legs. Creatine phosphokinase (CPK) was 3,1872. EMG displayed a myopathic pattern, while repetitive nerve stimulation was normal. MRI showed muscle swelling, mainly in the posterior compartment in the thigh. Other blood and autoimmunity test were non-contributory. Under fluid therapy and after sorafenib withdrawal, CPK and muscle strength improved. However, the systemic situation of the patient was considered terminal and palliative care was started, being transferred to a palliative facility.
Conclusion: Sorafenib can be related to cases of rhabdomyolysis and muscular diseases, as the present case show. It should be considered in cases of acute muscle weakness in patients under this treatment.
Disclosure: There are no conflicts of interest to disclose.

EPO-102

AChR- positive myasthenia gravis with persistent electrophysiological presynaptic pattern

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Background and aims: Myasthenia gravis (MG) and Lambert–Eaton myasthenic syndrome (LEMS) are autoimmune disorders of the postsynaptic and presynaptic neuromuscular junction, respectively. They are both characterized by muscle weakness and fatigability and differentiated on the basis of clinical, immunological and electrophysiological features.
Methods: Case Report
Results: A 26-year-old female, with multiple autoimmune disorders (i.e. hypothyroidism, systematic lupus erythematous, autoimmune hemolytic anemia), presented with eyelid ptosis, diplopia and lower limb weakness. Neurological examination revealed proximal limb weakness, eyelid ptosis and diplopia, exacerbated upon sustained activity. Deep tendon reflexes were normal and no autonomic dysfunction was observed. Repetitive nerve stimulation revealed findings suggestive of presynaptic neuromuscular transmission defect. However, acetylcholine receptor–binding antibodies (AChR-Abs) were positive at 324nM/L, while p/q type voltage-gated calcium channel antibodies were negative. Computed tomography of mediastinum was normal. Oncological screening was negative. The patient did not undergo thymectomy. Pyridostigmine was beneficial and steroid treatment resulted in marked improvement. During a 10-year follow-up, the electrophysiological presynaptic pattern is persistent while the titer of AChR Abs is positive.
Conclusion: In this case, the clinical pattern in combination with positive AChR-Abs, despite atypical presynaptic electrophysiological findings, set the diagnosis of MG. Although, our knowledge of cases with characteristics of both diseases is limited, acknowledgement of such cases is imperative. MG and LEMS have many clinical similarities and their distinction is important due to different therapeutic approaches and different associations with malignancies.
Disclosure: Nothing to disclose.

EPO-103

Persistent anti-Ri antibodies in non-tumor Lambert-Eaton Myasthenic Syndrome

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[1] Athens, Greece, [2] Aeginition Hospital, Athens, Greece

Background and aims: Lambert–Eaton myasthenic syndrome (LEMS) is an uncommon autoimmune presynaptic disorder of the neuromuscular transmission associated with antibodies towards voltage-gated calcium channel (VGCC) of P/Q-type. There is also a strong association with small cell lung cancer (SCLC) concerning about 50–60% patients with LEMS (tumor-LEMS).
Methods: Case Report
Results: A 68-year-old non-smoker female with diabetes mellitus, presented with a 6-month-history of progressive proximal lower limb weakness, weight loss and xerostomia. Neurological examination revealed predominant lower limb weakness with areflexia of upper and lower limbs. Repetitive nerve stimulation revealed presynaptic neuromuscular transmission defect and the titer of VGCC Abs was positive. Thus, the diagnosis of LEMS was set. A thorough work-up for an underlying neoplasm, including whole body PET-CT, was normal while testing for paraneoplastic antibodies revealed positive type 2 antineuronal nuclear antibodies (ANNA-2/anti-Ri). For the following two years, the clinical course was benign and non-progressive with a beneficial response to treatment. Although anti-Ri Abs remained persistently positive, malignancy has not been detected despite the thorough oncological screening.
Conclusion: Anti-Ri antibody is a paraneoplastic autoantibody with a strong association with lung, breast and gynecological tumor. Tumor-LEMS has rarely been associated with anti-Ri antibodies and other paraneoplastic autoantibodies. To the best of our knowledge, this is the first reported case of anti-Ri positive non–tumor LEMS. Oncological screening for LEMS is sufficient for two years after the diagnosis. However, due to persistent anti-Riseropositivity it may be prudent to continue screening up to four years as it applies to other paraneoplastic neurological syndromes.
Disclosure: Nothing to disclose.

EPO-104

Lambert-Eaton-Myasthenic-Syndrome as an adverse effect of RET inhibitor therapy: a case report

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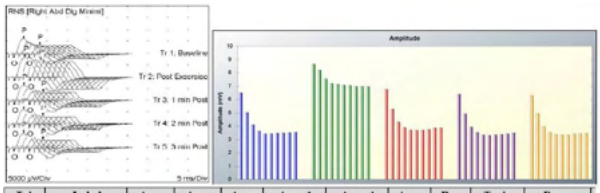
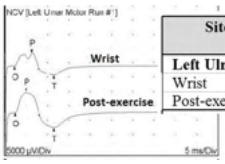
Background and aims: RET inhibitors are targeted therapies for advanced tumors with RET gen alterations, as RET-altered thyroid cancer. Several adverse effects have been described, such as hypertension, increased transaminases level or hyponatremia. Yet, there are no described cases reporting Lambert-Eaton-myasthenic-syndrome (LEMS) as an adverse effect of RET inhibitor therapy. We describe the 1st case of a patient undergoing RET inhibitor therapy who develop a Lambert-Eaton-myasthenic-syndrome.
Methods: Case report
Results: After lymph node disease progression in 2019, a 28 year-old woman with metastatic medullary thyroid carcinoma diagnosed in 2012, received treatment with BOS172738 (a selective RET inhibitor). After two weeks, the patient developed proximal weakness associated with myalgias, dysarthria, dysphagia, and dyspnoea. The physical exam showed proximal tetraparesis with conserved reflexes. A blood test showed negative onconeuronal, anti-acetylcholine-receptor, anti-MuSK and calcium-channel antibodies. The neurophysiological study showed normal sensory-motor nerve conductions, F waves and needle electromyography; however, repetitive nerve stimulation showed decrementing response with significant post-exercise facilitation, suggestive a presynaptic neuromuscular junction alteration: LEMS. After treatment with intravenous immunoglobulin, corticoids, 3,4-diaminopyridine and piridostigmina, the patient significantly improved. One week after continuing the treatment with BOS172738, the patient developed again a similar clinical myastheniform syndrome. Thus, the treatment with BOS172738 was discontinued.



Tria l#	Label	Amp 1 (mV) O-P	Amp 4 (mV) O-P	Amp % Dif	Area 1 (mV·ms)	Area 4 (mV·ms)	Area % Dif	Rep Rate	Train Length	Pause Time (min:sec)
Right Abd Dig Minimi										
Tr 1	Baseline	6,51	3,67	-43,6	23,09	13,16	-43,0	3,00	5	00:45
Tr 2	Post Excersise	8,66	7,23	-16,5	29,52	25,20	-14,6	3,00	5	01:00
Tr 3	1 min Post	6,77	3,90	-42,3	25,15	13,82	-45,1	3,00	5	01:00
Tr 4	2 min Post	6,40	3,57	-44,2	23,00	12,16	-47,1	3,00	5	01:00
Tr 5	3 min Post	6,30	3,56	-43,6	22,08	12,08	-45,3	3,00	5	00:00

Figure 1. Repetitive Nerve Stimulation in abductor digitis minimis (10 estimuli with 3Hz) shows a significant decriment (>10%) of compound muscle action potential with a significant increase of amplitude of post-exercise action potential



Site	NR	Onset (ms)	P-T Amp (mV)	O-P Amp (mV)
Left Ulnar Motor Run #2 (Abd Dig Minimi)				
Wrist		2,2	7,9	4,4
Post-exercise		2,3	12,1	6,8

Figure 2: Post-exercise facilitation. A low amplitude of motor ulnar nerve potential registered in abductor digitis minimis (chanel 1). A significant increase in amplitude post-exercise is observed.

Conclusion: As far as we know, this is the first described case suggesting an association between RET inhibitor therapy, a novel treatment for advanced tumors with RET gene alterations, and LEMS. Physicians should be aware of this possible adverse effect in patients who develop muscle weakness while undergoing RET inhibitor therapy.
Disclosure: Nothing to disclose.

EPO-105

Inflammasome inhibitors for the treatment of muscular dystrophies

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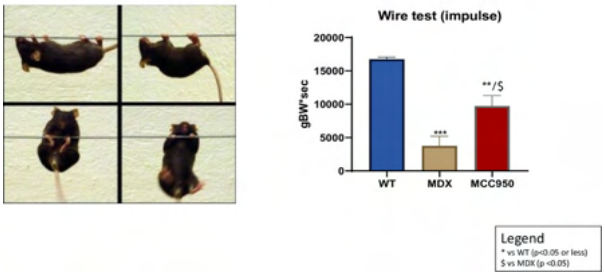
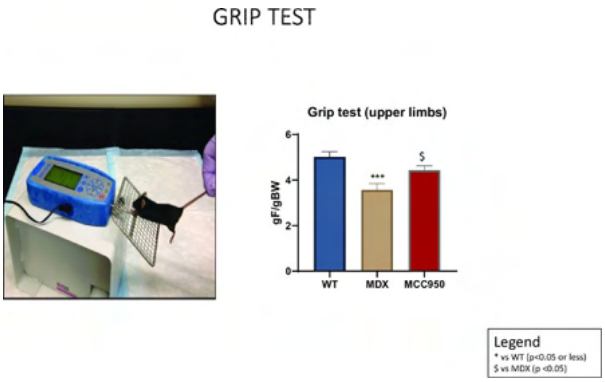
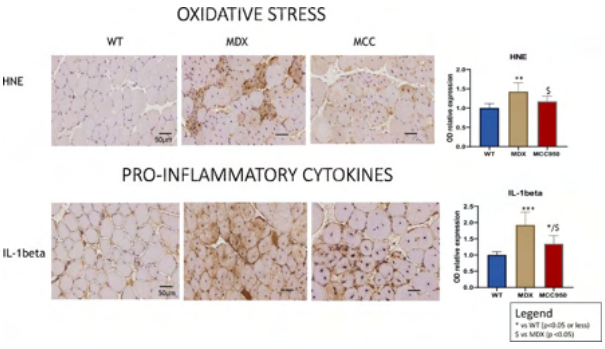
Background and aims: Duchenne muscular dystrophy (DMD) is the most frequent inherited human myopathy and one of the most devastating muscular dystrophies. Although dystrophin mutations represent the primary cause of DMD, it is the secondary processes involving persistent inflammation that likely exacerbate disease progression. Our group previously described the involvement of the NLRP3 inflammasome as having a major role in the deleterious inflammatory process worsening the dystrophic phenotype. Recently, MCC950 was discovered as an extremely potent, selective, small molecule inhibitors of NLRP3 and could thus be promising in muscle diseases with an inflammatory component.
Methods: Fourweekold mdx mice (n=6 per group) were orally treated with MCC950(mdxMCC950) 80mg/kg for eight weeks and compared with untreated (mdx) mice and to control mice. In vivo functional tests were carried out to measure the global force and endurance of mice. Ex vivo biochemical and molecular analyses were performed to evaluate the pathophysiology of the skeletal muscle.
Results: MdxMCC950 mice exhibited enhanced physical performance with an increase in both muscle force and endurance versus mdx mice (2.5fold for wire test, p=0.01; and 1.5-fold for grip test, p=0.04). In addition, MCC950 reduced oxidative stress (-20%, p=0.048 for HNE) and inflammation (-25%, p=0.047 for IL1). Finally, necrosis, embryonic myosin (a marker of muscle regeneration) and the number of small sized myofibers were reduced.



Wire test



Grip test



Inflammation

Conclusion: MCC950 improved significantly mice performances in vivo, counterbalanced excessive inflammatory and oxidative responses, mitigated necrosis and slowed down the myofibers degradation/regeneration turnover. This molecule could thus offer promising therapeutic prospect for managing DMD or other muscle and inflammatory disorders.
Disclosure: Nothing to disclose.

EPO-106

Distal Presenting Myasthenia Gravis – Eletrophysiologic Tests Role

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Background and aims: Myasthenia gravis (MG) is an autoimmune disease in which antibodies bind to acetylcholine receptors or to functionally related molecules in the postsynaptic membrane at the neuromuscular junction. It usually affects proximal limb, ocular or bulbar muscles, where distal extremity muscles are typically spared. Specific antibodies are found in majority of patients but in antibody-negative cases, neurophysiological tests and a characteristic response to therapy secure the diagnosis.
Methods: Clinical cases.
Results: Case 1: 66 years old male refer for evaluation of progressive bilateral footdrop. Four month before he had an episode of sudden binocular diplopia with spontaneous resolution. Clinically showed complex eye movement limitations and bilateral leg weakness with clear distal predominance with steppage gait. Slow repetitive nerve stimulation (RNS) showed decrement response in several muscles. Anti-AchR were negative and he responded to pyridostigmine treatment. Case 2: 80 years old female with progressive bilateral hand and proximal inferior limb weakness for five months. Neurological examination showed weakness particularly in extension of hands and fingers bilaterally, and also axial cervical. There were decrement in slow RNS in several muscles with improvement with pyridostigmine test and jitter in the single fiber EMG. Antibody testing was negative and treatment with pyridostigmine lead to clinical improvement.
Conclusion: Even though the history of ocular disturbances in first case and the proximal and axial limb involvement in both could have pointed to MG, the prominent distal weakness could have been misleading, so we conclude that neurophysiological studies were crucial to a timely and accurate diagnosis.
Disclosure: Nothing to disclose.

EPO-107

A clinical and kinematic evaluation of foot drop in myotonic dystrophy type I: a pilot study

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Background and aims: Myotonic dystrophy (DM1) is a multisystem disease that involves several organs including the brain and muscles. Foot drop, gait alteration, and high risk of falling are core features of the disease. Rehabilitative approaches may benefit from a deeper understanding of how foot drop impairs gait. This pilot study aims to evaluate foot drop by merging clinical and kinematic analysis.
Methods: A cohort of 39 patients with genetically confirmed DM1 and able to walk without any support was evaluated. Quantitative muscle test and 6-minute walk test (6MWT) were performed. In addition, 13 patients and 11 healthy controls (HC) underwent the 10-meter Walk Test while wearing kinematic sensors at the legs. An amplitude analysis and a power spectral density analysis of the ankle angles during gait were performed, conducting to a severity index (Norm2). Descriptive statistics, t-test, and correlation test were analyzed.
Results: A direct correlation was found between foot dorsiflexors strength (FDS) and 6MWT ($p<0.01$) in the DM1 cohort. The kinematic analysis differentiates well DM1 from HC. AR, PR, and Norm2 showed a good inverse correlation with FDS (r -0.86 $p<0.001$).
Conclusion: Foot drop is a core feature of DM1 and exposes patients to reduced mobility and a greater risk of falling. Dorsiflexors strength loss correlates with a poorer performance at functional outcomes such as 6MWT. The kinematic analysis may improve patients' stratification based on strength loss and functional capacity. These findings further clarify how foot drop affects gait and help to create a tailored rehabilitation program for each DM1 patient.
Disclosure: The authors report no conflicts of interest.

EPO-108

A rare inflammatory myopathy: long-term remission in two cases of Whipple Disease with muscle involvement

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Background and aims: Whipple disease, a rare infectious disorder involving multiple systems, represents an uncommon form of reversible myopathy.
Methods: We report two cases of Whipple disease with muscle involvement. The first is a 67-year-old male admitted for arthralgias and progressive lower limbs weakness. The second is a 68-year-old male presenting symmetrical lower-limb proximal hyposthenia, skin hyperpigmentation and gastrointestinal symptoms. A 5-year-long follow-up after diagnosis was performed.
Results: In both cases, proximal lower-limb muscular hypotrophy was found. CK values were normal, immune-rheumatologic screening tested negative. Electromyography showed mixed neurogenic and myopathic features. Total-body CT scans, spine and brain MRI were unremarkable. Muscle biopsy was performed: in the first patient it showed interfascicular macrophages with Periodic Acid Schiff positive inclusions. The second patient showed mild myopathic alterations. Polymerase Chain Reaction (PCR) for Tropheryma whipplei tested positive on both patients' muscle specimens; in one case also duodenum, faecal and saliva samples were positive on PCR. Oral Cotrimoxazole administered for two years gradually resolved first patient's symptoms. A relapse occurred one year after drug suspension, requiring adjunctive 12-months therapy; a stable remission was then achieved. second patient was treated with Cotrimoxazole for two years and remained in remission. At last clinical examination both patients were able to walk correctly and stand from chair and floor; a mild proximal
lower-limb hypotrophy was still evident.
Conclusion: Subacute progressive weakness with muscle wasting and multisystemic involvement should prompt an extensive search for treatable causes, including Whipple disease. In our cases, a long-term stable remission was observed after appropriate therapy.
Disclosure: Nothing to disclose.

Neuroepidemiology

EPO-109

Hospital morbidity from nervous system diseases in the Brazilian unified health system

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Background and aims: Hospital morbidity corresponds to the percentage distribution of hospital admission by groups of selected causes. The aim of this study was to describe the hospitalizations for diseases of the nervous system in Brazil from 2010 to 2019.
Methods: An ecological study was carried out in January 2021 from the health information of the Brazilian Health Unified System databases. All hospital admissions resulting from the international classification of diseases (ICD), chapter VI in Brazil from 2010 to 2019 were included. The main variables analyzed were sex, age, elective or urgency character, regime of hospitalization and geographic region. Descriptive statistics were performed though absolute (n) and relative (%) frequencies.
Results: A total of 1,668,876 hospital admissions were identified for diseases of the nervous system, with an increase from 11,799 in 2010 to 190,557 in 2019. Most patients were female (50.2%), aged between 50 and 59 years (15.6%) and urgent service (73.8%). Most frequent comorbidities, according to the ICD, were epilepsy (27.53%), nerve, root and nerve plexus disorders (14.1%) and transient ischemic stroke and related syndromes (12.3%). The largest number of hospitalizations occurred in the Southeast (43.04%), followed by the South (22.8%), Northeast (21.5%), Central-West (8.0%) and North (4.6%).
Conclusion: There was an increase in hospitalizations for diseases of the nervous system, with emphasis on the number of emergency care. In order to reduce hospitalizations, it is necessary to expand the screening and early diagnosis of such diseases.
Disclosure: No disclosures

EPO-110

Incidence of Multiple Sclerosis in Republic of Moldova in the year of COVID-19

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Background and aims: Multiple sclerosis is a chronic autoimmune, inflammatory and neurodegenerative disease of the central nervous system and the most common non-traumatic disabling neurological disease in young adults. In the latest decades, multiple sclerosis is increasing worldwide, especially in women. The objective of our neuroepidemiologic study was to review the incidence and sex ratio of multiple sclerosis in Republic of Moldova during 2020, in the year of the Covid-19 pandemic, and to verify if the worldwide crisis had an impact on the access to medical services for newly diagnosed multiple sclerosis patients.
Methods: Patients with ICD-10 code G35 were identified from the tertiary hospitals administrative data. Patient records were reviewed to include only cases with a definitive diagnosis according to the 2017 McDonald criteria. Incidence period covered one year, from 1 January 2020 to 31 December 2020.
Results: During the incidence period, 75 new MS diagnoses were made. The annual age-standardized incidence was 3.6/100 000 person-years (95% CI 3.2–3.9) in the age-group over 18 years old. The female to male ratio was 1.9:1, with the mean age 37,0 years (±1 year).
Conclusion: According to the country's estimates, the Republic of Moldova has an overall similar MS incidence rate as Central and Eastern Europe. Despite the onset of the Covid-19 pandemic, it did not impact the access to multiple sclerosis services for newly diagnosed patients.
Disclosure: No disclosures

EPO-111

Brain death in Mato Grosso – an epidemiological study about notifications

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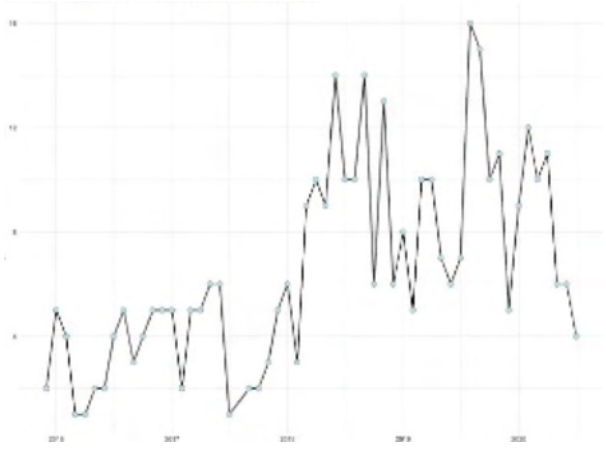
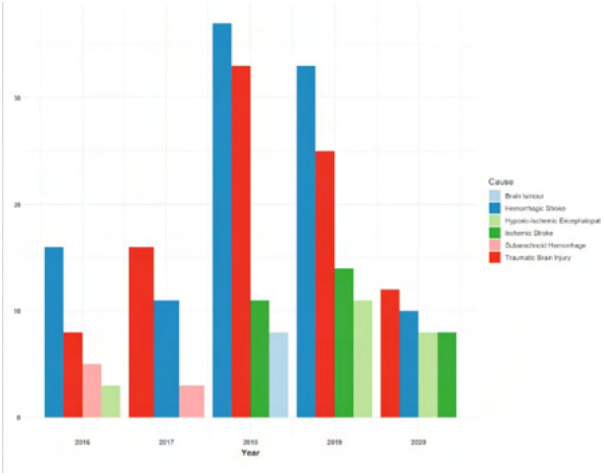
Background and aims: Transplantation and donation of human organs has instigated research aiming at the knowledge and understanding about the process of suspicion, definition and evaluation of brain death as well as the support and performance of transplantation and organ donation. In Brazil, publication of Resolution CFM 2173/2017, regulates the current criteria and mandatory procedures for brain death (BD) diagnosis, composed of two clinical tests, one apnea test plus complimentary exam. In Mato Grosso, the State Transplant Center (CET-MT) has been making efforts to disseminate the current CFM resolution, training courses for professionals working in ICUs and Urgency and Emergency environments, next to public and private hospitals. This study aims to analyze the epidemiological and demographic profile of brain death reports.

Methods: An observational cross-sectional study was carried out, collecting data contained in the registration notification of BD by CET-MT in the period from 2016 to 2020.

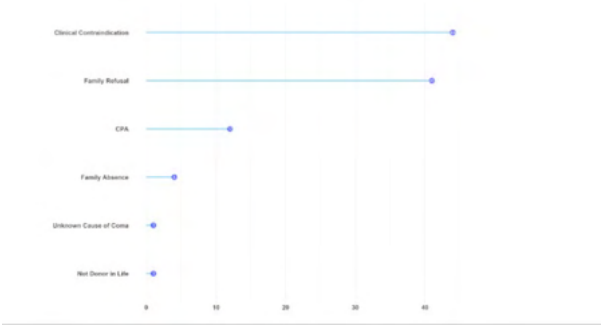
Results: From 367 BD suspected notifications at a period (Figure 1), 58.8% male, with mean age of 42,94 years. Figure 2 shows main causes of coma. Angiography and doppler were complementary exams most used and Figure 3 shows the main refusal reasons for donation. There were 108 CPAs in total, however, 96 occurred before brain death was confirmed and may have prevented some donations.



Monthly brain death notifications



Brain death etiology



Refusal reasons for donations

Conclusion: These results demonstrate that after the implementation of resolution CFM 2173/2017 added to training courses, was observed a considerable increase in notification. We understand that just knowing and analyzing those data will be possible to improve them.

Disclosure: No disclosures

EPO-112

Profile of 10 years of hospitalization for hydrocephalus in Brazil

S. Cabral [1], A. Ferreira Santos [1], P. Soares [1], M. Fernandes [1], A. Pereira [1], L. De Melo Ferreira [2], J. Nunes [1]
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Background and aims: hydrocephalus is a disorder caused by an excessive amount of cerebrospinal fluid in the cerebral ventricles and subarachnoid space.
Methods: it was evaluated the clinical and epidemiological profile of hospitalizations for hydrocephalus in Brazil, using a cross-sectional, retrospective study, based on data from the SUS Hospital Information System, from 2010 to 2019. The variables analyzed: sex, age group, race, region of residence and deaths.
Results: There were 161,890 hospitalizations for hydrocephalus, being 53.8% male. The most affected were under one year old (19.7%), the least affected over 80 (2.3%). 29% did not provide race; white (50,4%) and brown (44,7%) were the most frequent. The Southeast region had the highest number of hospitalizations (41.6%), while the North the smallest (5.6%). The death rate (number of deaths/100 hospitalizations) was 13.4%, the highest rate over 80 (31%) and the lowest in younger than one year (4.1%). Blacks had the highest death rate (19%); indigenous (12.2%) and white (12.3%) had the lowest. The Southeast, Midwest, North, South and Northeast had a death rate of 14.9%, 14.4%, 12.3%, 12% and 11.9% and between genders were similar, 13.4% for men and 13.5% for women.
Conclusion: The epidemiological profile of hospitalizations for hydrocephalus in Brazil is associated with male patients, aged less than one year, white race and residing in the Southeast. Deaths are more frequent over 80 years of age, black ethnicity and residents of the Southeast.
Disclosure: Nothing to disclose.

EPO-113

Alzheimer's disease mortality rate from 2007 to 2017 in the state of Rio Grande do Sul, South Brazil

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Background and aims: Alzheimer's disease is the biggest cause of dementia and one of the biggest sources of morbidity and mortality in the elderly population. It is marked by progressive loss of mental functions, such as loss of memory and language. This study aims to evaluate Alzheimer's mortality in the population of the brazilian state of Rio Grande do Sul.
Methods: Cross-sectional, descriptive and retrospective study, which evaluated the evolution of the mortality rate from Alzheimer's disease from 2007 to 2017 in the brazilian state of Rio Grande do Sul. Mortality rates were evaluated by age group, sex and race using the national database.
Results: It was observed that 1.5% of the total deaths in the state in the period were related to Alzheimer's disease, with 65.5% of the patients being 80 years old or more. Considering the decade, the mortality from this pathology increased by 123%. There was a 2:1 female to male ratio. About 92.3% of patients who died were white.
Conclusion: There was an increase in mortality from Alzheimer's Disease in the state of Rio Grande do Sul from 2007 to 2017, which may be related to greater life expectancy, improvement of the diagnostic criteria for the pathology and more access to health professionals in the region. This mortality increase is greater between the female population. In addition to that, the disease is still little analyzed epidemiologically in the country despite its progressive incidence, which is alarming and needs more attention.
Disclosure: Nothing to disclose.

EPO-114

Prevalence of latent tuberculosis infection in patients with multiple sclerosis

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Background and aims: The use of immunosuppressant drugs for treating multiple sclerosis (MS) increased in the last years. In those patients, the screening of latent tuberculosis infection (LTI) is recommended to avoid reactivations.
Methods: An observational, retrospective study was performed to analyze the prevalence of LTI in patients with MS who started an immunosuppressant treatment during the last two years. The LTI screening included a Mantoux test, if negative a Quantiferon was done. When a positive result was obtained, chest radiography was performed.
Results: 38 patients were included, 55% women, 84% with relapsing-remitting MS, mean age of 43 years (standard deviation (SD) 11.1) and a mean of six years (SD 9.12) after diagnosis of MS. 16% received the BCG vaccine and 8% had a previous tuberculosis infection. Mantoux was positive in 18% and Quantiferon in 0%. Only one patient had chronic changes in chest radiography and none had active disease. 66% of patients with LTI took isoniazid for nine months, and 34% rifampicin for four months. The LTI did not delay the immunosuppressant starting (59 days in LTI vs 90 in non-LTI, p=0.264), and no relapses happened during this period.
Conclusion: LTI is common in patients with MS and its treatment did not delay the start of MS treatment. Quantiferon test did not increase the sensitivity of Mantoux in the diagnosis of LTI.
Disclosure: This study was not financed.

EPO-115

Analysis of the cost and length of stay related to the placement, review and removal of ventricular shunt in Brazil

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Background and aims: The cerebrospinal fluid (CSF) shunt is a mechanical system that aims to drain the excess liquor from the cerebral ventricles. Its malfunction occurs at a rate of 40% even in the 1st year post-placement, generating the need for readmission to review or withdraw this system. Therefore, the current work aims to identify the costs and length of hospitalization added by procedures for the removal and review of ventricular shunt compared to those referring to its placement.
Methods: This is a descriptive cross-sectional study between January 2008 and May 2020. Information on hospital admissions in Brazil was used for placement, removal and review of cerebrospinal fluid derivation available in the SUS Hospital Information System.
Results: 112,200 patients were hospitalized due to placement, review or removal of ventricular shunt, generating a total expenditure of 390,600,935.06 reais with an average of 10.6 days of hospitalization for each patient. In isolation, placement generated a total expenditure of 351,517,598.22 reais and an average hospital stay of 10.8 days. The withdrawal or revision of the derivation were responsible for a total expenditure of 39,083,336 reais and an average hospital stay of 9.7 days.
Conclusion: It is concluded that procedures related to the malfunction of the CSF derivation, added a total expense of 39 million reais and increased the average hospital stay of these patients by 9.7 days. These results reiterate the importance of looking for ways to avoid complications related to this neurosurgical procedure.
Disclosure: HGRS

EPO-116

Epidemiological overview of stroke admissions in Brazil in 10-year time series: a comparative study

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Background and aims: Brain stroke is a recurrent emergency in Brazil, causing cognitive, sensory and motor alterations, depending on the particularities of the injury, resulting in hospitalizations.
Methods: It is configured as a cross-sectional descriptive study, with data from the SUS (Unified Health System) Hospitalization System, accessed through DATASUS. The period analyzed was from January 2010 to December 2019 in Brazil, comparing age, gender, and total expenditure of hospitalizations by SUS.
Results: In Brazil, 1,410,410 hospitalizations per stroke were recorded in the aforementioned period, resulting in a total of R$1,736,528,110.72 spent. The age group most affected was 60–79 years, with 716,507 (50,80%) hospitalizations, making use of 51,13% of the budget. The most affected sex was male (51.88%), especially from the age of 50, prevailing up to the age of 69, with 328,660 more hospitalizations. Above the age of 80, the female gender stands out in 41,573 admissions.
Conclusion: There was a substantial difference in stroke cases between men and women in the 50–69 age group, indicating a higher risk factor for developing strokes in males. However, the increase in occurrence in women over the age of 80 may be related to the lower life expectancy of men compared to women. The higher prevalence between 60 and 79 years of age explains the higher propensity to stroke found in older age groups. Finally, the expenditure demanded for this disease indicates that admissions for strokes significantly impact in Brazilian's health population and budget.
Disclosure: No members involved in this abstract present conflict of interest.

EPO-117

Stroke awareness and response in Chile: a transversal study using a telephone survey

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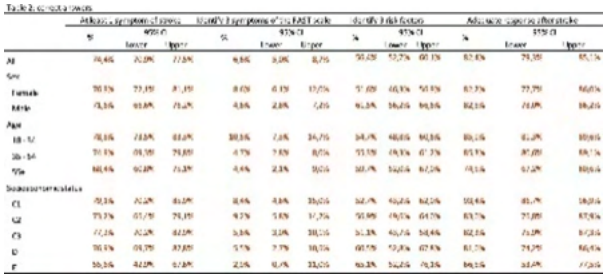
Background and aims: Stroke symptoms awareness and how to access to reperfusion therapies within the community has not been studied in Chile. We assessed stroke symptoms knowledge as well as stroke risk factors (RF) and the planned response among Chileans.
Methods: Closed-ended questions structured survey was telephonically applied. Probabilistic sample, random selection and stratification for region was used. 706 surveys were applied for a 3.7% standard error with 95% interval of confidence. Multivariate logistic regression model was used to assess the odds of identifying at least one stroke symptom and a good response to a recognized stroke. Frequencies and adjusted OR are presented.
Results: 74.4% (70.9–77.5) individuals recognized correctly at least one symptom. Only 6.6% (5–8.7) recognized the three symptoms of the FAST scale altogether. Mistakenly, headache was the most frequently selected symptom (44.2%) followed by difficult speaking (43.8%) and weakness of one arm/leg (38.1%). Identification of at least 1RF was seen in 97.9%. A good planned response was chosen by 82.4% (79.3–85.1). Variables associated with better recognition of at least one symptom were being women (AOR 1.49, 1–2.1), younger than 35 years (AOR 1.71, 1.1–2.7) and higher socioeconomic status (SES) (AOR 3, 1.5–6.2). Younger than 35 years was associated with a good planned response (AOR 1.95, 1.2–3.2) as well as higher SES (AOR 6.3, 2.4–16.5).

Table 1: demographic characteristics

	n(%)
Total	706 (100%)
Sex	
Female	354 (50.1%)
Male	352 (49.9%)
Age	
Mean (SD)	42.0 (15.5)
18 - 34	273 (38,7%)
35 - 54	270 (38,2%)
55+	163 (23,1%)
Socioeconomic status	
C1	109 (15,4%)
C2	186 (26,3%)
C3	167 (23,7%)
D	182 (25,8%)
E	62 (8,8%)



Conclusion: A quarter of Chileans do not recognize at least one symptom of stroke. Nevertheless, there is a good recognition of RF. There is need for strengthened educational campaigns especially in olders and with lower SES groups.

Disclosure: Research grant from Boehringer Ingelheim

EPO-118

Subclinical atherosclerosis and left ventricular function evaluation in patients with acute leukemia

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Background and aims: The aim of this study was to evaluate early changes in subclinical atherosclerosis and left ventricular (LV) function in patients with acute leukemia (AL) before and six months after chemotherapy treatment by measuring Intima-Media-Thickness(IMT) using Extracranian-Doppler(ECD), Ankle Brachial Index (ABI) and LV function using echocardiography.

Methods: We enrolled 40 patients with AL evaluated before and six months after chemotherapy. Blood pressure(BP), heart rate(HR), body mass index(BMI) were measured. The echocardiography and markers of subclinical atherosclerosis (IMT, ABI) were performed prior and six months after chemotherapy treatment. All parameters of LV function and markers of subclinical atherosclerosis were correlated with the age of the patients and type of AL.

Results: From all studied patients, aged 49.78±17.45, 21(52.5%) were patients with acute myeloid leukemia(AML) and 19(47.5%) were with acute lymphoblastic leukemia(ALL). 14(35%) patients were aged<45 and 26(65%) patients aged >45, 16(40%) were hypertensive patients, 7(17.5%) were diabetes patients and 17(42.5%) were smokers. There was a significant decreased in Left Ventricular Ejection Fraction(LVEF)(%) and Global Longitudinal Strain(GLS)(%) and a significant increase in IMT(mm) six months after chemotherapy ($p<0.001$). LVEF(%) was significantly decreased in AML patients and aged >45, six months after chemotherapy treatment ($p<0.05$).

Conclusion: We consider it is very useful to perform a careful analysis of both cardiac and vascular function before beginning chemotherapy, but also periodically, after initiation of chemotherapy treatment. Evidence of atherosclerotic changes and LV function are useful in preventing risk of developing cardiovascular events, and this may be influenced by the age of patients and the type of leukemia.

Disclosure: Nothing to disclose.

EPO-119

Global Warming and Neurological Practice: Systematic Review

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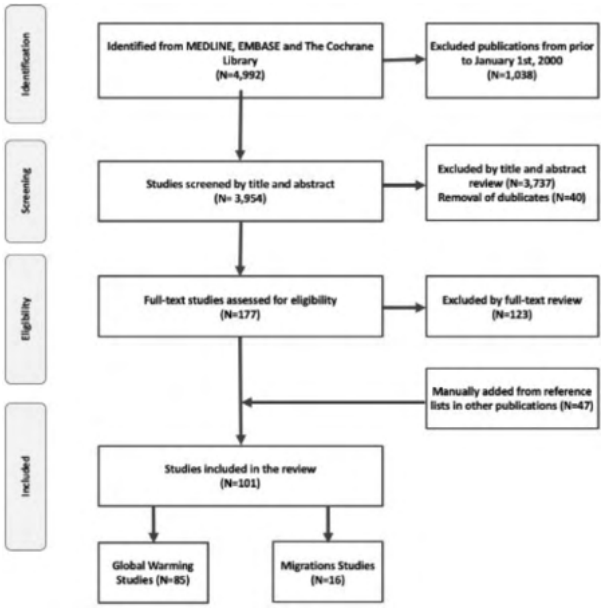
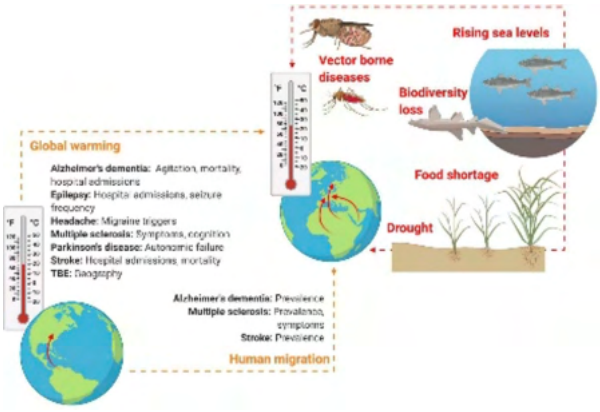
[1] *Department of Neurology, Copenhagen, Denmark,* [2] *Italy*

Background and aims: Climate change, including global warming, is expected to cause poorer global health and a rise in the number of environmental refugees. As neurological disorders account for a major share of worldwide morbidity and mortality, climate change and global warming are also destined to alter neurological practice; however, to what extent and by which mechanisms is unknown. We aimed to collect the available information on the effects of ambient temperatures and human migration on the epidemiological and clinical manifestations of major neurological disorders.

Methods: We searched PubMed and Scopus from January 1, 2000 to November 30, 2020 for human studies published in English addressing the influence of ambient temperatures and human migration on Alzheimer's and non-Alzheimer's dementia, epilepsy, headache and migraine, multiple sclerosis, Parkinson's disease, stroke, and tick-borne encephalitis (as a model disease for neuroinfections). The protocol was pre-registered at PROSPERO (2020 CRD42020147543).

Results: 101 studies met inclusion criteria, but we were unable to identify a single study addressing how global warming and human migration will change neurological practice. Still, extracted data suggested multiple ways by which these aspects might alter neurological morbidity and mortality in the future.





Conclusion: Significant heterogeneity exists across studies with respect to methodology, outcome measures, control of confounders and study design, but there is enough evidence to suggest climate change will affect the neurological practice of all major neurological disorders. Adequately designed studies to address this issue are urgently needed, which will require concerted efforts from the neurological community.

Disclosure: The authors declare no conflicts of interest.

EPO-120

Neurocysticercosis in a tertiary referral neurological hospital in Mexico City: evolution between 1995 and 2019

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Background and aims: Neurocysticercosis(NC) is a parasitic disease with heterogeneous presentations. Its clinical manifestations range from mild headaches to severe hydrocephalus. This diagnosis requires specialized imaging or studies not available in all the regions of undeveloped countries where this disease occur the most. (Del Brutto) That is why it is not easy to estimate true prevalence in large populations like Mexico. To do so, we measured the proportion of NC patient's hospitalization during the years 1995–2009.

Methods: Data were obtained from the National Institute of Neurology epidemiological service, using CIE-10 codification B.69 (NC). The age and gender of hospitalized patients were collected. Spearman's correlation and linear regression were used to assess the relationship between hospitalizations rates and calendar periods, and between mean age and calendar periods.

Results: In Neurosurgery, the NC patient's admission rate showed a decreasing trend was statistically significant ($r=-0.69$; $p<0.001$). Neurology service also showed a significant decrease in NC-admissions ($r=-0.68$; $p=0.001$). Mean age was 44.45 (±4.02). A significant positive trend was observed ($r=0.21$, $p<0.0001$). A positive strong correlation was found showing an increase in mean age (0.77 $p<0.001$). The prevalent gender was male (53%) and a total of 32 deaths were identified.

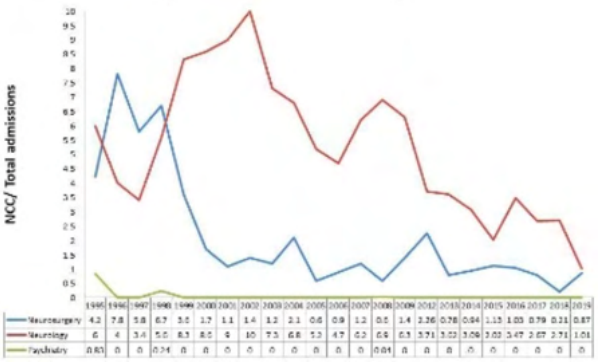
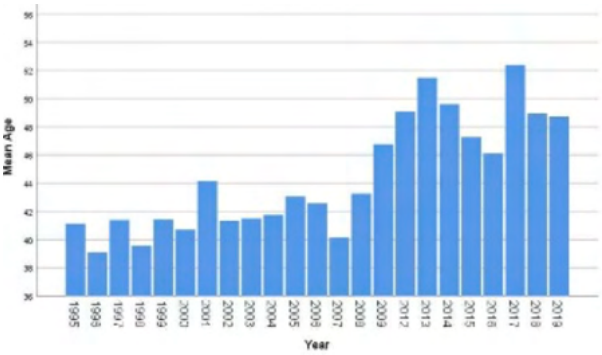


Figure 1. Proportion of NCC hospitalized patients between 1995–2019



Mean age by year

Conclusion: hospitalization. This data could be confirming the empirical observed tendency by neurologist all over the country of lower prevalence of NC but larger, nationwide studies are needed.

Disclosure: No disclosures are reported for the present study.

EPO-121

Long-term subcutaneous administration of apomorphine or insulin for Parkinson's disease or diabetes and skin event rates

K. Wells [5], S. Zhou [1], J. Engelhard [6], D. Oleske [2], B. Werner [3], M. Facheris [2], J. Zamudio [4]
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Background and aims: Safety data on long-term administration of continuous subcutaneous infusion of drugs for chronic conditions are limited. This study characterized the frequency and types of skin events occurring during this method of drug administration in real world settings.
Methods: We conducted a descriptive cohort study of new users of continuous subcutaneous infusion of apomorphine (CSIA, n=51) or insulin (CSII, n=257), aged 30+ years, for Parkinson's disease or diabetes, respectively, using a German health claims database. The skin event categories examined were: skin infections, skin nodules/localized swelling, local allergic/inflammation, and overall.
Results: The 24-month probability of an incident skin event was 40% in the CSIA cohort and 28% in the CSII cohort. The overall skin event rate (SER) was 42.0 per 100 person-years (PY) in the CSIA cohort and 43.3 per 100 PY in the CSII cohort. The most frequent skin events were: local allergic/ inflammatory skin reactions (CSIA: 78.3%; CSII: 58.1%) followed by skin infection (CSIA:21.7%; CSII 39.4%). Within 12 weeks after infusion start, a SER of 134.3 and 57.2 per 100 PY for CSIA and CSII cohorts respectively, was observed. The SER decreased over time in the CSIA cohort (12≤24 weeks, 151 per 100 PY; >52 weeks, 17.9 per 100 PY), but increased in CSII cohort (12≤24 weeks, 33.6 per 100 PY; >52 weeks, 43.3 per 100 PY).
Conclusion: Clinically important skin events are common throughout the administration of subcutaneous infusion of drugs but higher at initiation in the CSIA cohort than in the CSII cohort.
Disclosure: Drs. Oleske, Facheris and Zamudio are employees of AbbVie. AbbVie provided funding to IQVIA. Ms. Wells, Dr. Engelhard, and Ms. Zhou, are employees of IQVIA. Ms. Werner is an employee of Team Gesundheit.

Neuro-oncology

EPO-122

Painful ophthalmoplegia due to involvement of cavernous sinus region by malignant neoplasm: report of three cases

H. Silva Junior [1], B. Franchito [2], M. Sukessada [2], D. Gulhote [2], G. Barros [3], J. Silva [2], A. Barbosa Piffer [3], P. Fortunato [4], D. Ueno [4]

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Background and aims: Spread of tumor to intracranial structures is an infrequent and late manifestation of head and neck cancers. We report three cases of painful ophthalmoplegia due to larynx and parotid neoplastic involvement.

Methods: We report the cases in order to increase the visibility of metastases to the CS resulting in ophthalmoplegia. Data disclosure was authorized by the patients through an Informed Consent Form (ICF).

Results: A 47-year-old man presents right retro-orbital pain and progressive ophthalmoplegia five months after resection of laryngeal spinocellular carcinoma and local radiotherapy. A 44-year-old man, nine months after excision of spinocellular carcinoma of the larynx and subsequent radiotherapy, presents severe pain and paralysis of the left CN VI. Imaging exams showed involvement of CS (Figure 1 and 2). A 67-year-old woman with a tumoral mass in the left preauricular region. Biopsy revealed adenocarcinoma of the parotid gland. After total parotidectomy, the supra-omohyoid cervical ganglion was removed. Patient received radiotherapy for three months. Then, she presented a frontal and right temporal headache, more intense in the retro-orbital region. After one month, she developed complete CS syndrome, with the right CN VI being the first to be affected. MRI revealed a T1 hyperintense (figure 3) and T2 hypointense lesion with peripheral enhancement in cavernous sinus. All patients died despite treatment.

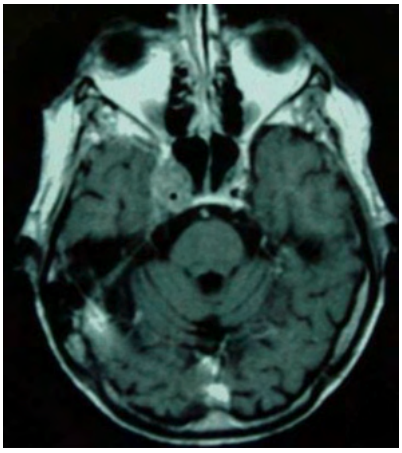

Figure 1: Expansive lesion (2,4x1,7x1,7 cm) in the cavernous sinus on the right (47-year-old patient).

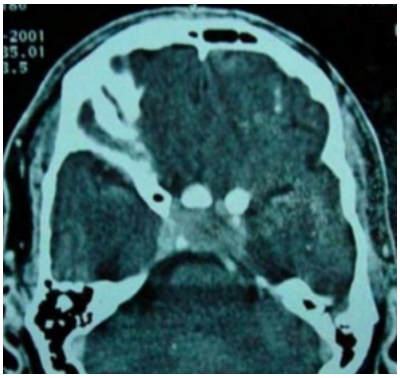

Figure 2: TC showing a hyperdense expansive lesion at the sella turcica's topography (44-year-old patient).

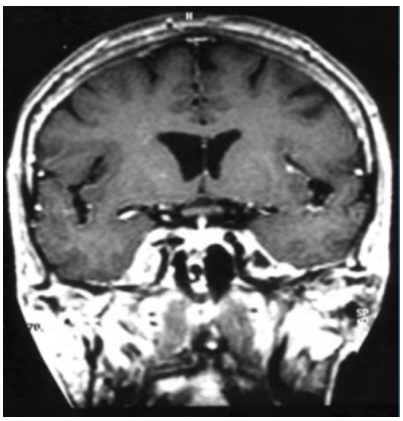

Figure 3: MRI showing T1 hypointense lesion in the right cavernous sinus.

Conclusion: In patients with painful ophthalmoplegia, the most common hypotheses are diabetic neuropathy and Tolosa-Hunt syndrome. CS involvement may be the first evidence of a distant head and neck disease.

Despite the poor prognosis, palliative care should be considered.

Disclosure: Nothing to disclose.

EPO-123

Coexistence of paraneoplastic autoimmune encephalitis and Lambert-Eaton myasthenic syndrome

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Background and aims: Paraneoplastic syndromes (PNS) are common, affecting up to 8% of malignancies. It is possible several antineuronal autoantibodies coexisting in a patient, mainly in the small cell lung cancer (SCLC). However, the coexistence of two PNS is rare.
Methods: Clinical Case
Results: A 72 years-old man, smoker, in March 2019 developed mania and persecutory delusions (1st-episode psychosis). Brain CT was normal. He started olanzapine. Months later the patient presented memory deficits and apathy. In February 2020 initiated dysphagia, dysphonia and muscle weakness of the lower limbs. Neurological exam showed bilateral ptosis, facial diparesis, weak palate movements, absent gag-reflex, generalized muscle weakness and weak deep tendon reflexes. Additionally, an asymmetric parkinsonian syndrome was observed. Repetitive stimulation EMG showed neuromuscular junction presynaptic dysfunction (CMAP increment during high-frequency stimulation). Antibodies P/Q type anti-VGCC, anti-SOX1 and anti-CV2/CRMP5 were present. CSF had 12 monocytes/mm^3 and normal protein levels. Both the EEG and the MRI were normal. The diagnostics of Lambert-Eaton myasthenic syndrome (LEMS) and probable paraneoplastic autoimmune encephalitis (PNAIE) were assumed. Thoracic CT scan showed mediastinal ganglia and dispersed nodular opacities; PET scan showed bilateral hypermetabolic nodules and suspected broncho-hilar metastization. Two fine-needle aspiration biopsies were negative for malignancy; a transthoracic approach was tried but aborted due to proximity to the aorta. The patient was treated with IV human immunoglobulins, pyridostigmine and prednisolone, with moderate clinical improvement.
Conclusion: We present a case of concomitant paraneoplastic syndromes: LEMS and PNAIE. Positive anti-SOX1 antibodies suggests the existence of a SCLC, reinforcing the need for a histological diagnosis to proceed treatment.
Disclosure: The authors declare no conflict of interests.

EPO-124

Neurological manifestations in the late postoperative period in children operated with cerebelar astrocytoma

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Background and aims: Cerebellar pilocytic astrocytoma is the most common type of benign tumor located in the cerebellum in children, and postoperative after-effects can prevent recovery treatment, these children frequently need care assistance.
Methods: Prospective study of late postoperative neurological manifestations (≥ 2 years after intervention) in 14 children (aged 7–18 years) operated on with cerebellar pilocytic astrocytoma between 2012–2018, who were not subjected to radiotherapy or chemotherapy.
Results: The most affected age: 10–14 years (42.9%), followed by 7–9 years (37.7%), then 14–18 years (21.4%). Location in the cerebellum: vermis – 10 children, vermis and both hemispheres – 1, right cerebellar hemisphere – 1, left cerebellar hemisphere – two children. Postoperative syndromes: posterior fossa – eight children (57.1% [II 60.33–44.17], p=0.05); moderate and severe motor deficit – 10 (71.4%, [II 83.47–59.33], p=0.07), mild – one child; expressive language deficit – five (35.7% [II 50.31–24.69], p=0.05), spontaneous conversation – three (21.4%, [II 32.37–10.43], p=0.06). At the localization in the vermis persisted the deficit of emotional control (anxiety, panic attacks, aggression), as well as eating disorders – five (35.7%); emotional lability – 12 (85.7%); cognitive disorders – 12 (85.7%); vegetative disorders (bradycardia, orthostatic syncope, hypotension, hyperhidrosis, flatulence, asthenia, insomnia) – 12 (85.7%) children; and in the left cerebellar hemisphere – dysmetry and dysdiadokokinesis.
Conclusion: In children operated on with cerebellar astrocytoma in the postoperative period, neurological manifestations with moderate and severe motor deficit persist, as well as the symptoms of the vegetative nervous system, negatively influencing their recovery.
Disclosure: Estimation of neurological manifestations in the postoperative period in children operated on with cerebellar pilocytic astrocytoma who have not undergone radiotherapy or chemotherapy.

EPO-125

Perioperative Levetiracetam for seizure prophylaxis in brain tumor patients with focus on neurocognitive functioning

E. Konrath [1], F. Marhold [2], W. Kindler [3], F. Scheichel [2], B. Popadic [2], K. Blauensteiner [3], B. Calabek [3], E. Freydl [3], M. Weber [4], R. Ristl [5], K. Hainz [3], C. Sheriff [2], S. Oberndorfer [3]

[1] St. Pölten, Austria, [2] Department Neurosurgery, University Clinic St. Pölten, KLPU, Austria, [3] Department Neurology, University Clinic St Pölten, KLPU, Austria, [4] Department of Biostatistics, KLPU, Austria, [5] Center for Medical Statistics, Informatics and Intelligent Systems, Austria

Background and aims: The effectiveness of prophylactic antiepileptic drug in seizure naive brain tumor patients remains a matter of controversial debate. According to pharmacokinetics, side effects and potential drug interactions, current choice is Levetiracetam (Lev). The objective of this study was to examine neurocognitive functioning of seizure naive brain tumor patients receiving antiepileptic drug levetiracetam perioperatively.
Methods: This prospective, observational study included radiologically suspected brain tumors in patients, who were routinely planned for surgery. Patients (18<90y), who were included, received Lev three days before until seven days after surgery as seizure prophylaxis. Cognitive performance (NeuroCogFX), Lev plasma-levels, hematotoxicity, side-effects as well as QoL (Qolie31) were recorded preoperative before and after onset of Lev, 5–7 days postoperative and 21 days at follow-up without Lev.
Results: Mean age of the 43 patients which met the inclusion criteria was 61 years (gender ratio m/f: 2/3). Most frequent postoperative histology was malignant glioma (58%). Most frequent side effect related to study drug was somnolence (24%). No significant changes in cognitive performance and QoL were seen after onset of preoperative Lev treatment. There was a significant improvement of NeuroCogFX total-score at time point 4 ($p=0.004$) compared to baseline. Cognitive subdomains which exhibited significant improvement were working memory and figural memory. Overall score Qolie31 showed simultaneous improvement patterns as cognitive performance ($p<0.001$).
Conclusion: Significant cognitive improvement, as well as improvement in Qol was detected in the postoperative phase, which was attributed to the debulking effect of surgery. Levetiracetam showed no cognitive or hematological toxicity in the perioperative phase of brain tumor patients.
Disclosure: Nothing to disclose.

EPO-126

Time to start treatment of brain tumors in the Brazilian unified health system

J. Nunes [1], P. Soares [1], M. Fernandes [1], S. Cabral [1], A. Pereira [1], L. De Melo Ferreira [2], A. Ferreira Santos [1]

[1] Savador, Brazil, [2] Neurocirurgia, Salvador, Brazil

Background and aims: The current standard treatment of malignant tumors of the brain includes surgery, radiotherapy and/or chemotherapy. The type of injury, in addition to other risk factors, influence for the choice of the therapeutic modality that has a better risk and benefit ratio, in order to maintain quality of life for the patient.
Methods: This is a cross-sectional section from 2015 to July 2020, with secondary data published by the Ministry of Health and extracted from the PANEL-Oncology-Brazil, being observed: first therapy instituted, diagnosis, year of treatment and time to start treatment.
Results: Data from 26,237 cases were collected, of which 17,491 had information about the treatment. Of these, 47.7% were treated up to 30 days after diagnosis, 18.1% from 31 to 60 days and 34.2% after this period. However, there was a reduction in the time elapsed from diagnosis to treatment, 65.6% made up to 60 days in 2015 and 92.3% in 2020. There was an increase in surgeries, from 19.9% in 2015 to 69.3% in 2020, and a reduction in radiotherapy, 67.1% in 2015 to 21.5% in 2020.
Conclusion: There was an increase in the proportion of tumor of uncertain or unknown behavior, probably due to the greater availability and request of immunohistochemistry, reflecting with an increase in surgeries as the 1st therapy instituted and reduction of the time between diagnosis and treatment.
Disclosure: Nothing to disclose.

EPO-127

"Villaret's Mimic Syndrome" as presentation of cerebral metastasic ovarian cancer

L. Palliotti [1], V. Gajate Garcia [1], M. Garcia Ruiz [1], L. Portocarrero Sánchez [1], M. Sánchez Boyero [1], A. Marcos Dolado [1], E. Lopez Valdes [2], R. Ginestal [1]
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Background and aims: Involvement of Cerebral Nervous System (CNS) related to ovarian cancer is uncommon, but due to the rise of the survival rate, its incidence has increased. We present an atypical clinical manifestation of CNS metastatic involvement due to ovarian cancer.
Methods: Description of a clinical case of a patient admitted in the Neurology Department of "Hospital Clinico San Carlos" of Madrid, Spain.
Results: A 73-year-old woman with a diagnose of a high grade serous ovarian cancer treated with chemotherapy and surgery, presented a 3-week history of progressive dysphonia, dysphagia and gait instability. The neurological exam showed involvement of left cranial nerves IX, X, XI and XII as well as ipsilateral Horner syndrome and truncal ataxia without motor or sensory involvement. The clinical picture was compatible with Villaret's syndrome (VS) even though truncal ataxia exceeded this syndrome. Therefore, a head and neck computerized tomography was performed, but it did not show relevant findings. On the contrary, a cerebral Magnetic Resonance revealed a left posterolateral bulbar metastasis (figure 1, figure 2) and meningeal carcinomatosis. With the neuroimaging findings, the final diagnose was medulla oblongata metastasis that resembles a VS, being remarkable the lack of involvement of sensory and motor central pathways.

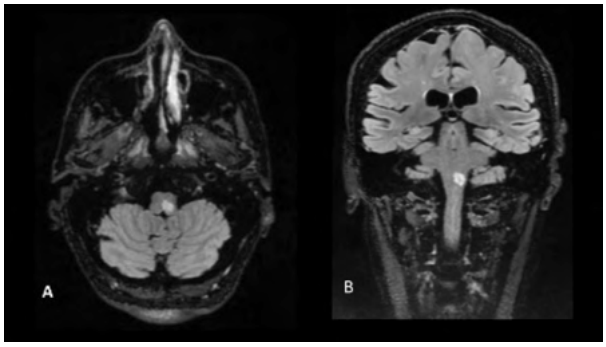

figure 1. Axial (A) and Coronal (B) FLAIR- weighted brain MRI shows an hyperintense lesion in the left posterolateral medulla oblongata

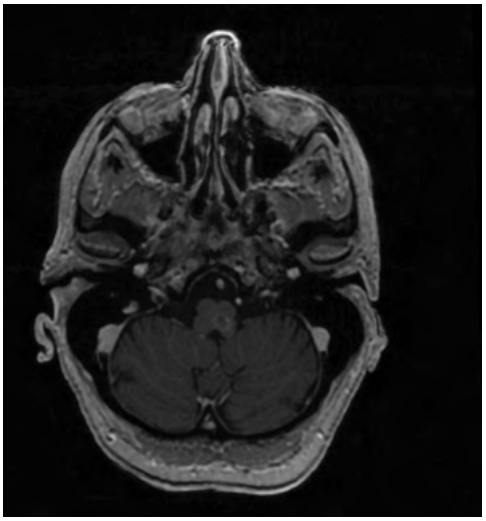

Figure 2. Axial postcontrast T1-weighted brain MRI shows a contrast-enhanced lesion in the left posterolateral medulla oblongata

Conclusion: Ovarian cancer might spread to CNS. Bulbar involvement not always implies involvement of sensory/motor central pathways simulating, therefore, a peripheral involvement of cranial nerves such as VS.
Disclosure: The Authors declare that there is no conflict of interest.

EPO-128

Predictors of hormonal dysfunction in the postoperative of non-functioning pituitary macroadenomas: a systematic review

A. Rossetti Junior [1], I.C. Salles [1], G. Rocha [1]
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Background and aims: The surgery for adenoma resection represents the main therapeutic choice for non-functioning pituitary adenomas (NFPAs), aiming at decompression and preservation of important neural structures. Several specific and perioperative factors of the patient are predictive of postoperative pituitary function. Therefore, the present study seeks to evaluate the prognostic factors for hormonal dysfunction in the postoperative period of patients undergoing surgery for resection of NFPAs.
Methods: A search for scientific articles in english, published between the 2010 and 2020, was carried out in the PUBMED database. The terms: "Pituitary Macroadenoma"; "Hypothalamus, Adenohypophyseal Disorders" and "Surgery" were used as descriptors. Patients diagnosed with NFPA without previous hypersecretory hormonal dysfunction and undergoing surgery for tumor resection were the main inclusion criteria for the study.
Results: Out of 684 studies obtained, 33 articles were selected for full reading and only six studies were eligible for the present study. The articles demonstrated the presence of hyposecretory dysfunctions in the preoperative period at the resection of the NFPA. Also, it was observed the persistence of the condition in the postoperative period and/or the appearance of new deficiencies of the hormonal axis. Hypogonadism, hypothyroidism and adrenal insufficiency were the main deficiencies present in all the studies analyzed. The first two being the worst prognosis for recovery.

Authors	Country of origin	Year	Sample (n)	Mean Age (years)	Sex (Male)	Study Duration (years)
Najmaldin et al	Iran	2019	71	50.6 ± 1.4	46	3
Poli et al	Italy	2019	109	56 ± 17	71	3
Chen et al	China	2010	385	51	203	8
Dallapiazza et al	United States	2014	80	56.6 ± 13	38	4
Yildirim et al	Turkey	2015	160	48.46	88	5
Little et al	United States	2019	169	57.6 ± 13	99	2

General characteristics of the selected studies

Conclusion: The review identified the tumor size, the invasion of the cavernous sinus and the presence of pituitary deficiencies in the preoperative period as factors that influence the postoperative period of patients undergoing NFPA resection.
Disclosure: The study is not receiving funding/assistance from any commercial organizations and the authors declare that they have no conflicts of interest.

EPO-129

Evidences of rearrangement of primary motor cortex in patients with low-grade glioma: a systematic review

R. Silva [1], F. Dos Santos Souza [2], M. Furlan Chaves [3], L. Monteiro [4], M. Braz [5], F. Tabarelli [6], F. Nascimento [7], A. Oliveira [8]
[1] *Recife, Brazil,* [2] *Universidade do Estado de Mato Grosso, Cáceres, Brazil,* [3] *Campo Grande, Brazil,* [4] *Federal University of Alagoas, Alagoas, Brazil,* [5] *Municipal University of São Caetano do Sul, São Paulo, Brazil,* [6] *Federal University of Pernambuco, Recife, Brazil,* [7] *State University of Ponta Grossa, Paraná, Brazil,* [8] *Neuroscience Centre, Luanda, Angola*

Background and aims: Compensatory mechanisms resulting from the phenomenon of neuroplasticity are present in patients with low-grade gliomas (LGG). When located in the primary motor cortex, the neural reorganization of motor activity to other areas of the brain may favor the maintenance of motor activity and avoid neurological deficits. Thus, the present study seeks to assess where the motor activity moves in patients with LGG.
Methods: The search strategy used the medical subject headings (MeSH) neuroplasticity, low grade gliomas and primary motor cortex. The databases included in the systematic review were PubMed and BVS. Following PRISMA guidelines, four studies were included were classified in low grade glioma-related neuronal changes in the primary motor cortex.
Results: From the studies analyzed, three demonstrated mechanisms of neuroplasticity in primary motor cortex. These, one reported higher activation of the contralateral motor area and contralateral supplementary area, respectively. In another study, the supplementary area contralateral to the tumor (SMAa) was more activated in the postoperative period in 40 patients, in addition to a clinical trial revealed a functional deviation of more than 10mm in relation to the motor cortical level. Although, only a retrospective study did not demonstrate migration of motor activity, making surgical resection unfeasible.
Conclusion: Although the primary cortex motor is a unimodal area and absent of a parallel alternative route, which would justify its low plasticity, studies have shown higher activation and consequent neural reorganization in the postoperative period of the contralateral supplementary area and contralateral primary motor area, respectively.
Disclosure: Yes

EPO-130

New onset hyposmia and hypogeusia as presentation of anti-Ma2-associated encephalitis with mediastinal seminoma

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[1] Neurología, Madrid, Spain, [2] Neurology. Hospital General Universitario Gregorio Marañón, Madrid, Spain, [3] Movement Disorders Unit, Madrid, Spain, [4] Madrid, Spain

Background and aims: Anti-Ma2-associated encephalitis is a paraneoplastic disorder characterized by limbic, diencephalic and/or brainstem dysfunction. It is mostly related to testicular germ-cell tumors. Hyposmia and hypogeusia are not typical presentation symptoms. We present a case of anti-Ma2-associated encephalitis with mediastinal seminoma presenting with new onset hyposmia and hypogeusia.

Methods: A 23-year-old man complains of two weeks history of progressive hyposmia and hypogeusia. In addition, he noticed an increased appetite, asthenia and erectile dysfunction. He did not present seizures, cognitive impairment or behavioral changes. Neurologic examination was normal and Montreal Cognitive Assessment scored 29/30.

Results: A cranial CT showed hipodensity in both mesial temporal lobes. A cranial MRI showed bilateral hyperintense signal on FLAIR images in mesial temporal structures, uncus, amygdala, hypothalamus, fornices and lentiform nuclei compatible with limbic encephalitis. EEG was normal. Testicular ultrasound showed bilateral testicular microcalcification. Body CT showed a thymus size increase. 18-FDG PET-CT revealed anterior mediastinal increased metabolic activity. Serum anti-Ma2 antibodies were positive. A thymectomy was carried out. The pathological study confirmed a mediastinal seminoma. Eventually, the patient developed progressive amnesia and seizures refractory to anti-epileptic drugs and corticoids. Cyclophosphamide and chemotherapy achieved clinical stabilization sustained after 18 months follow-up.

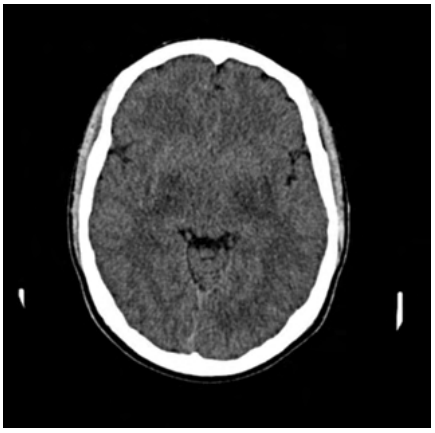

Image 1. Cranial CT.

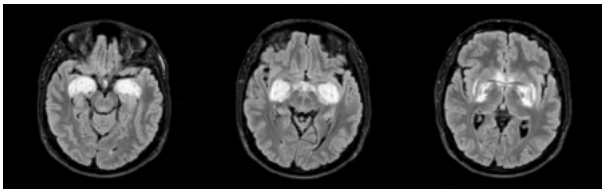

Image 2. Cranial MRI.

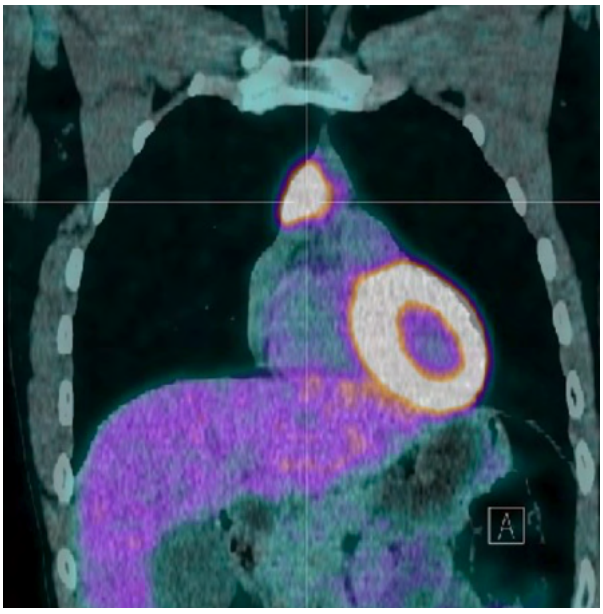

Image 3. 18-FDG PET-CT.

Conclusion: A case of anti-Ma2-associated encephalitis with mediastinal seminoma presenting with new onset hyposmia and hypogeusia is described. To our knowledge, this is the first well-documented case of hyposmia and hypogeusia as presentation symptoms of anti-Ma2 encephalitis. Rhinencephalon involvement confirms the central origin of hyposmia. Although rare, an extragonadal germ-cell tumor should be considered in anti-Ma2 encephalitis tumor screening.

Disclosure: Nothing to disclose.

Neuro-ophthalmology/neuro-otology

EPO-131

2 novel mutations in the SETX gene causing recesive ataxia with oculomotor apraxia type 2

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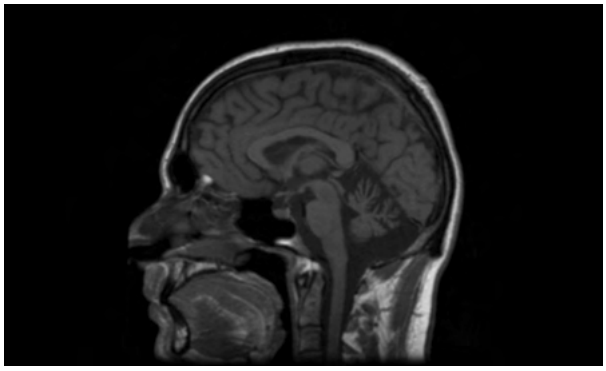
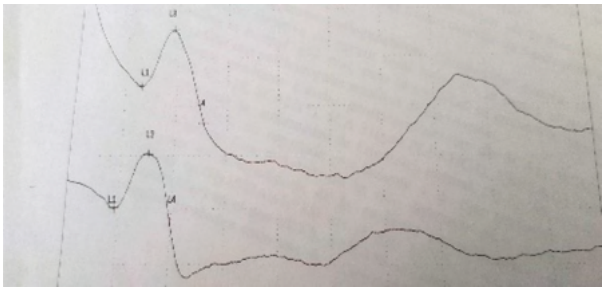
Salamanca, Spain

Background and aims: Senataxin protein, coded by the SETX gene is expressed in the brain, spinal cord, and muscles. The mutation in the gene is responsable of some different disorders: a juvenile onset of amiotrophic lateral sclerosis with autosomic dominant inheritence (ALS4), and a severe ataxia with oculomotor apraxia type 2 (AOA2).
Methods: We expose two case reports with two novel mutations in the SETX gene causing recesive ataxia with oculomotor apraxia type 2.
Results: In the index patient, we detected, in heterozigosis, the probably patogenic variant c.6182T>C (p.Leu2061Ser) and the uncertain significance variant c.4748del (p.Gly1583Alafs*10) variants. This same mutation were presents in the affected brother of our patient. We studied as well our patients' parents and the rest of siblings, for making an adequate aggregation study. The oldest sister had no mutations, while the youngest was carrier exclusively for the c.4748del variant (p.Gly1583Alafs*10). The detected variants in the index case come from each parent (trans configuration).



In the brain MRI we appreciate cerebellar atrophy with involvement of both hemispheres and vermix



In SETX gene, we detected, in heterozigosis, the probably patogenic variant c.6182T>C (p.Leu2061Ser) and the uncertain significance variant c.4748del (p.Gly1583Alafs*10) variants. This same mutations were presents in his affected brother.

Conclusion: Ataxia with oculomotor apraxia type 2 is a disease that involves a cerebellar ataxia, peripheral neuropathy and oculomotor apraxia. In the clinical report we present, we can observe the conjuntion of these clinical features in a young man. The cause is a mutation in the SETX gene.
Disclosure: I have nothing to disclose.

EPO-132

Cervical Vestibular Evoked Myogenic Potentials in Idiopathic Intracranial Hypertension

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Background and aims: Idiopathic intracranial hypertension (IIH) is raised intracranial pressure without any identifiable etiology. The inner ear structures are susceptible to cerebrospinalfluid (CSF) pressure changes because of connections between the CSF space and the labyrinth to explain the audiovestibular symptoms, suchas pulsatile tinnitus or dizziness, reported in 50% to 60% of these patients. The aim of this study was to investigate the vestibular functions using cervical vestibular evoked myogenic potentials in IIH.
Methods: Cervical vestibular evoked myogenic potentials werere corded in 30 patients with IIH before lumbar puncture. 30 healthy volunteers constituted the control group. The latenciesof peaks p13 and n23 and peak-to-peak amplitude of p13–n23were measured.
Results: Responses were gathered bilaterally from all healthy controls. In 30 patients with IIH, 49 responses could be gathered from 60 tests (81.7%). The potential was absent bilaterally in fiveand unilaterally in one patient. When recorded, the latency and amplitude values of the responses of the patients were not significantly different from the healthy controls (p=0.005). A correlation between CSF pressure and response persistence could not be determined.

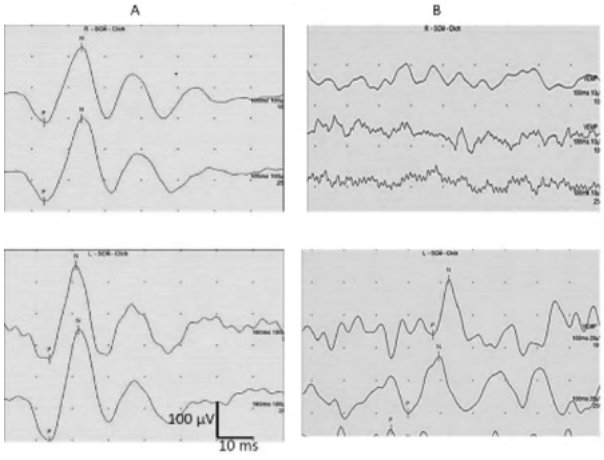

Figure 1: A. p13, n23 potentials recorded from a healthy control from the right (upper row) and left (lower row) sternocleidomastoid muscles B. Recordings from a patient with idiopathic intracranial hypertension without prominent potentials from either

Conclusion: Cervical vestibular evoked myogenic potentials are affected in patients with IIH and the main finding is the absence of the responses. Increased intracranial pressure causing sound transmission changes within the inner ear can affect the saccular afferents and may end up with absent responses on air-conducted cVEMP recordings. To comment on the correlation between the CSF pressure and cVEMP changes, successivecVEMP recordings with longitudinal CSF pressure monitoring seem necessary.
Disclosure: Nothing to disclose.

EPO-133

The impact of Covid-19 pandemic on idiopathic intracranial hypertension patients

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Background and aims: The COVID-19 pandemic became a challenge to maintain care for patients with idiopathic intracranial hypertension (IIH). We aimed to find out how they were affected during lockdown.

Methods: 30 IIH patients admitted to hospital during the COVID-19 pandemic were studied. Their demographic, neuro-ophthalmologic findings were evaluated. World Health Organization-5 Well-Being Index (WHO-5), The EUROHIS-QOL 8-item index, National Eye Institute Visual Functioning Questionnaire (NEI-VFQ-25), Headache Impact Test (HIT-6), Covid-19 Anxiety Scale were used to assess QoL and pandemic associated anxiety. Age, sex and body mass index (BMI) matched volunteers constituted the control group.

Results: Apart from the Covid-19 Anxiety Scale and the NEI-VFQ-25 color vision subscale, all test scores were impaired in IIH patients. General vision, distance vision and social function subscale scores of the NEI-VFQ-25 were lower in patients with low visual acuity (logMAR 0.1). Patients with perimetric MD 9 and papilledema grade three had higher HIT-6 scores than patients with perimetric MD<9 and papilledema grade <3.

Conclusion: Both vision-specific and overall QOL was reduced in patients with IIH. Headache disability was more prominent in patients with severe clinical features of raised intracranial pressure. Anxiety caused by COVID pandemic was not different from the healthy controls.

Disclosure: Nothing to disclose.

EPO-134

Cerebral venous thrombosis presenting as paroxistic positional vertigo: a case report

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Background and aims: Cerebral venous thrombosis (CVT) can be manifested through a wide range of neurological syndromes, depending on thrombosis' site and extension, which leads to diagnosis delays. The most common symptom, and often the first, is headache. Vertigo is a rare presentation; when present is usually associated with other signs of cerebellar dysfunction.

Methods: Case report

Results: A 43-year-old woman, with no prior medical history, on combined oral contraceptive since 2007, was admitted to the emergency department with acute vertigo, occipital headache, nausea and vomiting, triggered by cephalic movements on the horizontal plane. She denied pulsatile tinnitus, transitory visual disturbances or others. On examination, she had a central left facial palsy with normal fundoscopic test. Positional maneuvers at 30º triggered a symptomatic geotropic direction-changing horizontal nystagmus, suggesting a BPPV due to canalolithiasis of the left horizontal canal. The barbecue maneuver brought immediate symptomatic relief and significant nystagmus reduction. Brain CT venography revealed sigmoid sinus and jugular vein thrombosis with parietal bilateral SAH. No intraparenchymal lesions were found on the MRI. A comprehensive prothrombotic study revealed Ro/SSA and La/SSB autoantibodies, with lymphocytic infiltration on salivary glands biopsy. She was started on anticoagulant therapy with enoxaparin for the first two weeks and then dabigatran 150mg twice daily.

Conclusion: We describe an atypical presentation of CVT, with positional nystagmus responsive to repositioning maneuvers, in a patient with Sjogren Syndrome. In this case, in the absence of intraparenchymal lesions, the BPPV-like presentation could be explained by a venous overload and congestion of ipsilateral inner ear structures following CVT.

Disclosure: No disclosures.

EPO-135

A rare case of Vogt-Koyanagi-Harada Syndrome as a relapse-remitting multiple sclerosis comorbidity

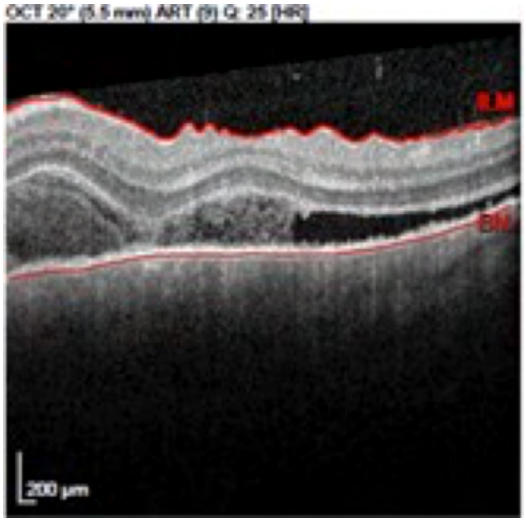
J. Dionísio [1], R. Basto [2], Â. Da Conceição Rosa de Abreu [3], A. Rêgo [4], C. Figueiredo [4], S. Delgado [5], F. Batista [6], S. Vieira [6], B. Grima [6], M. Bernardo [2], R. Manaças [7], M. Santos [3]

[1] Neurology, Lisboa, Portugal, [2] Ophtalmology, Lisbon, Portugal, [3] Neurologia, Amadora, Portugal, [4] Amadora, Portugal, [5] Serviço de Neurologia, Lisboa, Portugal, [6] UDIMS, Lisbon, Portugal, [7] Neurorradiology, Lisbon, Portugal

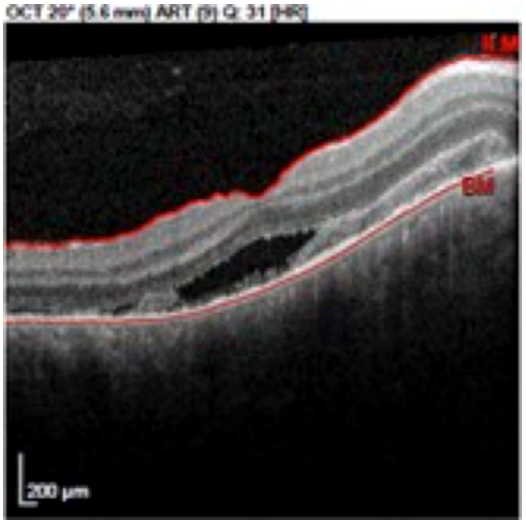
Background and aims: Vogt-Koyanagi-Harada Syndrome (VKHS) is a multisystemic granulomatous autoimmune disease affecting the uvea, meninges, and the auditive and tegmental systems, typically presented as a bilateral posterior uveitis. Only one literature case presents it as a multiple sclerosis (MS) comorbidity.

Methods: Case report

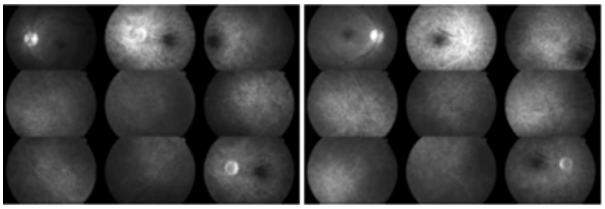
Results: A 47 years-old female with a relapse-remitting MS diagnosis, treated with interferon beta-1a, maintaining clinical and radiology activity, presents with a two-day history of bilateral painful severe visual acuity deficit (left eye 20/70, right eye 20/25), with initial innocent funduscopic examination, no relative afferent pupillary defect and mild left ocular hyperemia. With the hypothesis of bilateral optic neuritis, she was treated with methylprednisolone. The neuroaxis and orbits MRI excluded acute optic nerves involvement or new demyelinating lesions and visual evoked potentials were normal. After initial partial clinical improvement, she developed a new visual decline one week later. Cerebrospinal fluid presented 70 mononucleated cells. Ophthalmological re-evaluation with optical coherence tomography documented bilateral serous detachment pouches, choroidal precipitates and a neurosensory retinal detachment with macular involvement. Suspecting VKHS, a new methylprednisolone course was started, followed by prednisolone. The diagnosis was confirmed by fluorescein angiography. Interferon was switched to rituximab.



Optical coherence tomography re-evaluation (left eye)



Optical coherence tomography re-evaluation (right eye)



Fluorescein angiography (left and right eyes)

Conclusion: While optic neuritis is a common manifestation in MS, it is important to recognize atypical characteristics, to consider alternative diagnosis in MS patients presenting with new clinical signs and to remember MS' association with other autoimmune comorbidities. We highlight the rarity of the association of MS and VKHS and that the disease modifying treatment choice was based in its efficacy in both diseases.

Disclosure: The authors declare that they have no conflict of interest.

EPO-136

Abstract Withdrawn

EPO-137

Acute ophthalmoplegia associated with anti-GQ1b antibodies

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Background and aims: Anti-GQ1b antibodies are classically associated with Miller Fisher syndrome, which is characterized by ophthalmoplegia, ataxia and areflexia. Variants of this syndrome have been described, such as Bickerstaff brainstem encephalitis and acute ophthalmoplegia (AO). AO most commonly presents with relatively symmetric bilateral ophthalmoplegia, ptosis and facial palsies, although isolated cranial neuropathies have also been reported.
Methods: Case report
Results: A 66-year-old woman complained of bilateral temporal headache with progressive worsening over the course of two weeks, followed by the appearance of binocular diplopia. No previous infection or predisposing factor were identified. Bilateral abduction paresis, worse on the left eye, as well as bilateral supraversion paresis and ptosis were observed. Tendon reflexes were present and there were no signs of encephalopathy or ataxia. Brain MRI and repetitive nerve stimulation were normal. Serologic testing, including anti-acetylcholine receptor and anti-ganglioside antibodies, was ordered. CSF revealed a normal cell count but mild hyperproteinorraquia (72mg/dL). Considering the possibility of an inflammatory disorder, oral corticosteroids were initiated. Resolution of the headache and diplopia was observed in a few days. Laboratory results finally revealed positive Anti-GQ1b IgG antibodies, leading to the diagnosis of Acute Ophthalmoplegia associated with anti-GQ1b antibodies.
Conclusion: The presence of headache, hyperproteinorraquia and a complex ophthalmoplegia, with a normal MRI, led to the suspicion of an inflammatory cranial neuropathy. Even in the absence of ataxia or areflexia, anti-GQ1b antibody testing should be pursued. AO is a particularly challenging diagnosis as it may mimic other cranial neuropathies as well as neuromuscular junction and muscle disorders.
Disclosure: Nothing to report.

EPO-138

A history of panic attacks as a predictor of functional dizziness after benign paroxysmal positional vertigo

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Background and aims: Benign paroxysmal positional vertigo (BPPV) may be trigger to functional dizziness (FD). FD is frequent associated with anxiety disorders. There is little published data on correlations between panic attacks (PA), BPPV and FD.
Methods: The study involved 56 patients (50 women) aged 18 to 65 years with posterior canal BPPV, according to the criteria of the Barany Society. After successful treatment of BPPV with repositioning maneuvers patients filled out questionnaires and were re-examined one month later. We used Dizziness Handicap Inventory (DHI), Vertigo Symptom Scale Short form (VSS-SF), Digital analog scale of fear (from 0 to 10). Depersonalization-Derealization Inventory (DDI), PHQ-9, GAD-7 and PHQ-15. A history of PA was identified according to the DSM-5 diagnostic criteria.
Results: The cohort was divided into two groups according to the presence (25 patients, group 1) or absence (28 patients, group 2) of history of PA. Group 1 had more intensive dizziness ($p<0.05$), higher depression, somatization, derealization ($p<0.05$), fear and anxiety ($p<0.01$) during an attack of dizziness (table 1). FD occurred in 17 patients (32.1%) one month after BPPV. The prevalence of history of PA was significantly higher in patients with FD than without it (82.4% vs 30.5%). A history of PA in patients with BPPV increases the incidence of FD by 20.75% (Yates corrected Chi-square=10.44, $p=0.001$).

	Group 1 n=25	Group 2 n=28	p-value
Age	49,5 [42; 55,5]	52 [44; 59,5]	0,4
Vertigo symptoms			
DHI	56 [44; 72]	50 [28; 60]	**0,045**
DHI-F	20 [16; 30]	20 [10; 24]	0,1
DHI-E	16 [12; 22]	12 [8; 18]	**0,01**
DHI-P	18 [12; 22]	14 [10; 20]	0,1
VSS	18 [13; 27]	13 [9,5; 19]	**0,02**
VSS-V	10 [7; 15]	8,5 [6; 15,5]	0,2
VSS-A	7 [5; 12]	4 [2; 8]	**0,001**
Psychometric scales			
DDI	16 [12; 39]	12 [8; 21]	**0,04**
PHQ-9	10 [5,5; 18]	6 [2; 11]	**0,02**
GAD-7	8 [5; 15]	4,5 [1,5; 8]	**0,003**
PHQ-15	11 [9; 16]	9 [5; 12]	**0,04**
Digital analog scale of fear	8 [5; 10]	5 [2; 8]	**0,004**

Data are presented as median [lower quartile; upper quartile]

Table 1. Data of clinical and psychological testing of patients with BPPV

Conclusion: Patients with a history of PA have a more intense emotional response during a vertigo attack and a higher frequency of FD.
Disclosure: Nothing to disclose.

EPO-139

Non-arteritic anterior ischemic optic neuropathy (NAION) in young and older patients: the same entity?

J.M. Prieto [1], J. Losada Domingo [1], G. Agirre Beitia [1], W. Sifontes Valladares [2], M. Galdós Iztueta [3], V. Fernández Rodríguez [1], A. Rebollo Pérez [1]
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Background and aims: Non-arteritic anterior ischemic optic neuropathy (NAION) is the most common cause of optic neuropathy in adults. Its pathogenesis remains unclear, a genetic predisposition together with classic cardiovascular risk factors is believed to play an important role. It has also been hypothesized whether the entity could be different in younger or older patients.
Methods: We describe the clinical characteristics of 15 young patients (<50 years) with NAION – group I – and compare them to a group of over-50 (117 patients) – group II – from a tertiary hospital database.
Results: The gender distribution was similar in both groups: 77% men (group I) vs 56.3% (group II), p=0,23. No difference was observed in terms of cardiovascular risk factors – hypertension, diabetes, dyslipidemia or smoking habit. When analysing associated pathologies, such as autoimmune, neoplastic or heart disease, no difference was seen. Hypercoagulable states were found in two patients in group II (1,7%). Mean visual acuity in young people was better than in older people (0.4 vs 0.3; p=0.05). Involvement was bilateral in the same proportion. There was no significant difference in radiological findings between the groups. Patients in group I were more likely to have a pathological OCT (76.9 vs 52.1%, p=0.08).
Conclusion: In our series, no difference was observed in terms of cardiovascular risk factors or associated pathology, in the same line as other previous publications. This could justify a greater importance of the anatomical/genetical factor in the etiopathogenesis of the NAION.
Disclosure: Nothing to disclose.

EPO-140

Pseudo-spontaneous nystagmus in a patient with horizontal semicircular canal cupolithiasis

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[1] Neurology, Vienna, Austria, [2] Otolaryngology, Vienna, Austria

Background and aims: Benign paroxysmal positional vertigo (BPPV) is characterized by an exclusive transient position-induced nystagmus. However, few cases of pseudo spontaneous nystagmus (PSN) in BPPV of the horizontal semicircular canal (HSC) have recently been described, for which a canal blockage (canalith jam) is held responsible. We report the rare case of a patient with cupolithiasis of the HSC who presented with atypical horizontal spontaneous nystagmus (SN).
Methods: Case Report
Results: A 61-year-old patient presented with acute vertigo accompanied by nausea and unsteady gait. There was no hypacusis, tinnitus or pre-existing diseases. Neurological examination and video-oculography were normal, except for a high frequent SN to the left with low amplitude. Video-head impulse test, caloric tests and rotational tests yielded normal VOR-function. Cranial MRI was unremarkable. As Pagnini-McClure-maneuver induced a bilateral apogeotropic horizontal nystagmus, being stronger in left-ear-down position, cupolithiasis of the right HSC was diagnosed. Gufoni- and head shaking maneuvers subsequently transformed cupulolithiasis to canalolithiasis of the right HSC and ultimately led to the disappearance of the atypical spontaneous and positional nystagmus.
Conclusion: Based on the normal VOR function in our patient, we suspect a different pathomechanism than the common canalith-jam theory for the genesis of PSN in our patient with BPPV. We propose that a particular attachment of the otolith to the cupula and the physiological inclination of the HSC in the roll-plane induce a continuous cupula stimulation. Atypical nystagmus characteristics (low amplitude, high frequency) may be helpful in the differentiation between SN from unilateral vestibular neuropathy and cupulolithiasis-associated PSN.
Disclosure: Nothing to disclose.

EPO-141

Spectral features of postural sway in persistent postural-perceptual dizziness

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Background and aims: Previous studies in phobic postural vertigo patients showed characteristic frequency changes in body sway fluctuations, raising the question whether similar spectral changes can be also observed in the recently defined syndrome of persistent postural-perceptual dizziness (PPPD).
Methods: Static balance was assessed in 61 PPPD patients and 33 healthy controls during quiet stance on a force platform under different visual and proprioceptive feedback conditions. Postural sway was analyzed by means of time (sway area and standard deviation) and frequency domain metrics. The latter was based on comparisons of the percentage of energy in each of three frequency bands: low (0–0.5 Hz), middle (0.05–2 Hz) and high frequency (2–20 Hz).
Results: Time domain metrics deteriorated significantly from condition one through condition four in patients and controls. Spectral changes, however, were more abundant in PPPD subjects than in controls. Patients showed increased low frequency, but decreased high frequency spectral power in condition three as compared to condition two. Dizziness Handicap Inventory (DHI) score was positively correlated with middle frequency and negatively correlated with low frequency fluctuations.
Conclusion: We conclude that PPPD patients exhibit a time domain sway pattern in different conditions which is grossly similar to that of controls. However, two conditions with equal sway area, namely standing with eyes closed on firm surface and standing with eyes open on foam, show unique differences in their spectral content in PPPD patients. Finally, perceived severity of dizziness was associated with greater body oscillations in the middle frequency band.
Disclosure: Nothing to disclose.

EPO-142

Sonographic and ophthalmic assessment in patients with IIH

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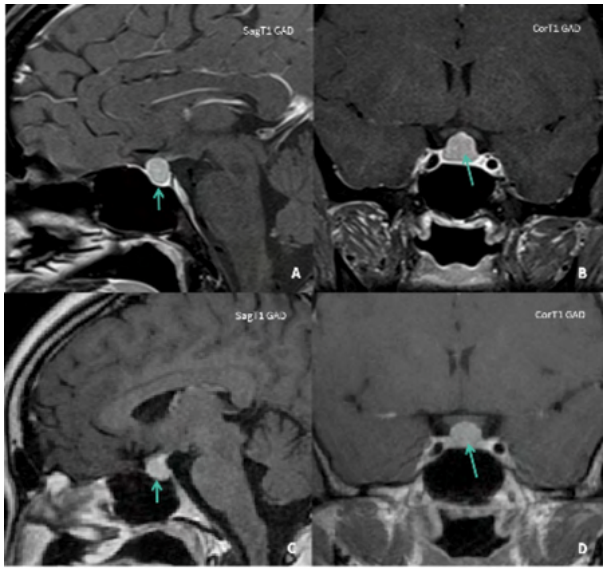
Background and aims: Idiopathic intracranial hypertension can compromise the optic nerve and aggravate the quality of life of patients. Objectives were to assess the value of ONSD and ODE for the detection of IIH and evaluate the validity of ophthalmologic and ultrasound parameters and clinical symptoms in monitoring the disease course of IIH.
Methods: This prospective, single-center, case-control study with 18 definite IIH and seven probable patients and 19 controls. Each participant underwent general medical, ophthalmologic, and neurological examination. included visual acuity assessment, by means of the Snellen chart (following correction), computerized static perimetry, perimetry threshold, and fundus examination, and sonographic assessment of optic nerve.
Results: ONSD was significantly enlarged bilaterally among individuals with IIH (6.2±0.73 (4.8–7.8mm)) compared to the controls (4.99±0.54 mm) ($p<0.001$). Bilateral papilledema (ODE) was found in 36/50 eyes of the patients in the IIH group at the initial visit and in none of the controls. Under six months of therapy, IIH patients showed a significant reduction after six months [6.2 mm (5.59–6.0), $p=0.024$]. Similarly, six months later ODE was 0.20mm (0.0–1.5). Moreover, in accordance with this finding, we observe a significant reduction of blurry vision but the persistence of other visual disturbances. In the subset of (follow-up group) IIH patients, we found persistence of increased ICP.
Conclusion: In summary, our study confirmed that TOS and opthalmological parameters are a valuable non-invasive method to detect and monitor elevated ICP in IIH.
Disclosure: Nothing to disclose.

EPO-143

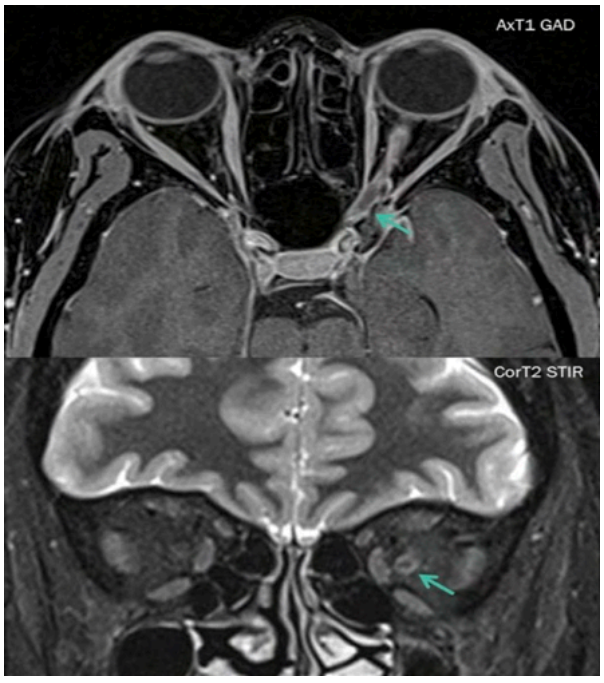
Anti-MOG bilateral optic neuritis and suspicion of a compressive pituitary macroadenoma: the relevance of semiology

S. Delgado [1], J. Dionísio [1], C. Figueiredo [1], J. Ramos [2], R. Fonseca [3], T. Baptista [4], M. Santos [1]
[1] *Neurology, Amadora, Portugal,* [2] *Neurology, Lisboa, Portugal,* [3] *Endocrinology, Amadora, Portugal,* [4] *Neuroradiology, Amadora, Portugal*

Background and aims: History and examination are essential in evaluating a patient with visual loss. Rapid progression is typical of optic neuritis and unilateral or bilateral painful severe visual deficit with optic disc oedema is the hallmark of anti-myelin oligodendrocyte glycoprotein (anti-MOG) disease. Pituitary macroadenoma compressing the optic chiasm generally presents with slowly progressive painless bitemporal hemianoptic defect. In the event of pituitary apoplexy, visual loss is sudden but generally associated with sudden headache and ophthalmoplegia.
Methods: Case report
Results: A 37-year-old puerperal woman presented with left retro-ocular pain exacerbated by eye movements followed in the next day by left monocular visual deficit (20/100), bilateral optic disc oedema (confirmed by OCT), left pupillary afferent defect, dyschromatopsia, and no peripheral visual field defects on confrontation. MRI revealed a pituitary enlargement (13x11x9mm) suggesting a macroadenoma with superior optic chiasma deviation and left optic nerve discrete thickening and gadolinium enhancement. Corticosteroids lead to sustained improvement of visual acuity, with unspecific changes on follow-up PEC. Further investigation revealed hyperprolactinemia (423ng/mL), unremarkable CFS (no oligoclonal bands), negative anti-aquaporin 4 and positive anti-MOG antibodies, leading to the diagnosis of anti-MOG disease. At three months, prolactin was normal, MRI disclosed a slight reduction in pituitary dimensions and the patient is still under surveillance with the hypothesis of pituitary hyperplasia related to pregnancy/lactation versus asymptomatic non-secreting macroadenoma.



Initial MRI (A and B) showing pituitary enlargement suggesting a macroadenoma (arrow) with superior optic chiasma deviation; and control MRI at three months (C and D) showing a slight reduction in pituitary dimensions (arrow) with minor chiasmal compression.



Initial MRI showing discrete thickening and gadolinium enhancement of left optic nerve (arrow), suggestive of left optic neuritis.

Conclusion: In this case with two concurrent possible entities, semiology lead to the cause of acute symptoms ant its successful treatment. Careful laboratory and pituitary imaging interpretation during pregnancy/lactation is crucial.
Disclosure: Nothing to disclose.

Neurorehabilitation

EPO-144

The effects of Transcutaneous Electroneurostimulation on low back pain

M. Al Zamil [1], N. Kulikova [2]
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Background and aims: To study the dynamics of low back pain after the application of various modalities of transcutaneous electroneurostimulation (TENS).
Methods: 60 patients with severe low back pain were studied. The severity of pain syndrome according to VAS was 7±0,15 points in average. The duration of the disease is from two weeks to a month. The prevalence of pain syndrome according to the McGill pain questionnaire (MPQ) was 29.6 ±0,25 points. At the same time, it averaged 15.6±0,15 points in the sensory class and 9.8±0,21 points in the affective class. 15 patients received only drug therapy. In addition to drug therapy, 15 patients underwent a course of low-frequency high-amplitude TENS (LF), 15 patients underwent a course of high-frequency low-amplitude TENS (HF) and 15 patients underwent a combined course using HF-LF TENS.
Results: As a result of treatment against the background of drug therapy, pain syndrome with VAS regressed by 27% and with MPQ by 39%. In patients who underwent HF TENS, the pain syndrome according to the VAS decreased by 53% and according to the MPQ by 63%. After LF TENS pain syndrome regressed by 56% with VAS and by 67% with MPQ. With the combined use of LF and HF TENS, the reduction in pain syndrome had the most pronounced effect and amounted to 76% by VAS and 79% by MPQ.
Conclusion: HF TENS and LF TENS are significantly effective in the treatment of low back pain. The most maximal analgesic effect is achieved with the combined use of HF and LF.
Disclosure: Nothing to disclose.

EPO-145

Efficiency of transcutaneous electroneurostimulation in complementary treatment of fibular tunnel syndrome

M. Al Zamil [1], N. Kulikova [2]
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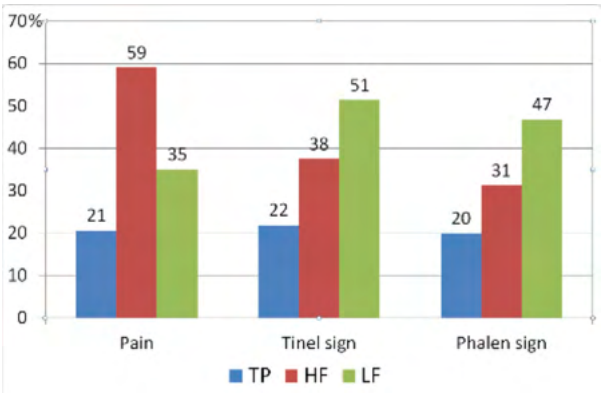
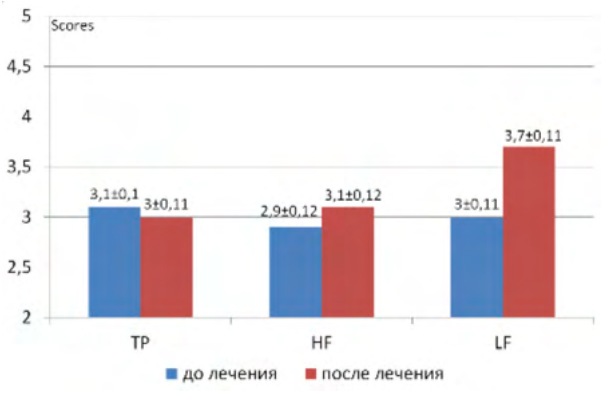
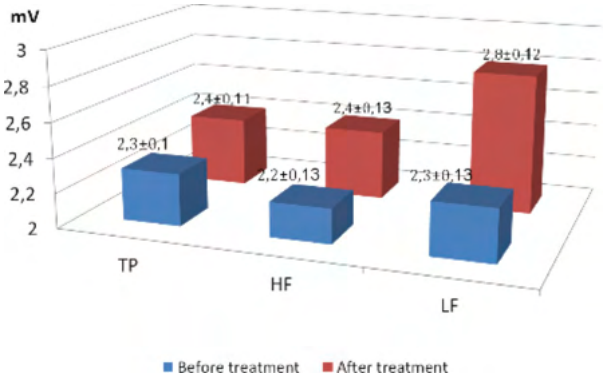
Background and aims: Comparative analysis of the effectiveness of traditional pharmacotherapy (TP) - control group and its combination with tow variants of transcutaneous electroneurostimulation (TENS) in treatment of patients with fibular tunnel syndrome (FTS) was done.
Methods: 60 patients studied with fibular tunnel syndrome. 20 patients underwent only TP. In addition to TP, 20 patients underwent High frequency-low amplitude (HF) TENS and 20 patients -low frequency-high amplitude (LF) TENS.
Results: A more pronounced decrease in pain syndrome was noted on the HF background and averaged 59%. The maximum decrease in Tinel and Phalen signs was observed after LF and decreased on average by 48 %. Motor deficit decreased by 23% only after LF, but not after HF. The improvement of the electromyography characteristics of affected peroneal nerve was noted only after LF.



Dynamics of pain syndrome and Tinel and Phalen signs after treatment of FTS by TENS



Improvement of ankle dorsflection in treatment of FTS by TENS



Increasing of amplitude muscle response of affected peroneal nerve in electromyography after TENS

Conclusion: Regression of pain, Tinel and Falen signs and motor deficit were more during and after treatment by TENS. LF frequency TENS are most effective in treatment of motor and sensory deficits, but HF TENS are most effective in treatment of pain. Regression of neurophysiology changes was noted only after LF TENS.
Disclosure: Nothing to disclose.

EPO-146

TENS leads to greater regression of motor deficits in the treatment of facial paralysis

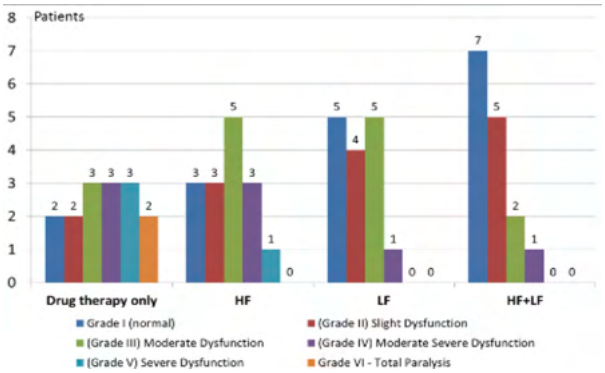
M. Al Zamil [1], N. Kulikova [2]
[1] *Amman, Jordan,* [2] *Moscow, Russian Federation*

Background and aims: In this work, a comparative study was carried out between high-frequency low-amplitude (HF) and low-frequency high-amolitude (LF) transcutaneous electroneurostimulation (TENS) in the treatment of facial nerve neuropathy.
Methods: 60 patients with severe neuropathy of the facial nerve were studied. 15 patients underwent drug therapy for a month. In addition to drug therapy, 15 patients underwent a course of low-frequenc high-amplitude TENS, 15 patients underwent high-frequency TENS and 15 patients underwent a combined course with the use of low-frequency and high-frequency TENS. The house brackman scale was used to determine the severity of motor deficits in the facial muscles on the side of the affected facial nerve. In all patients, the motor dedicits was assessed as severe.

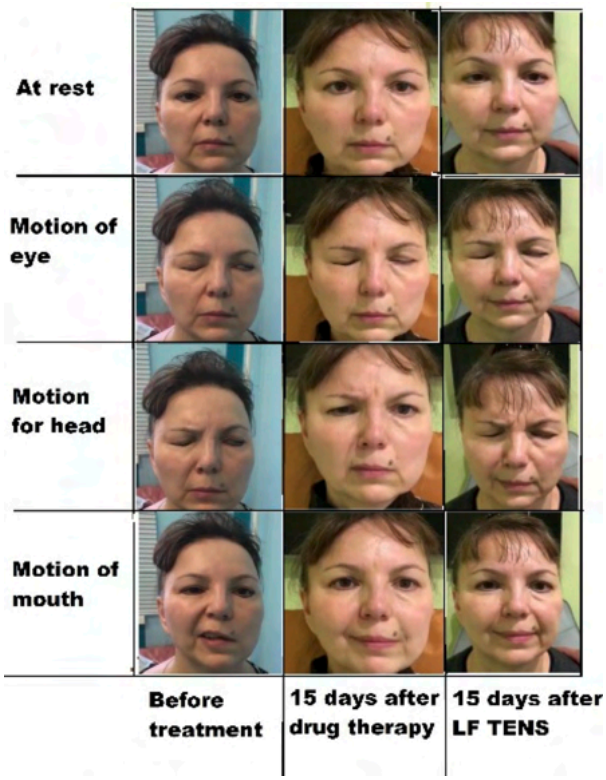
	Frequency	amplitude	duration	waveform	
LF	1 Hz	10-25 mA	200 mcs	monopolar (square)	
HF	100 Hz	5-10 mA	50 mcs	monopolar (square)	

Characteristics of TENS

Results: Total regression of motor deficit was observed in two patients in the group taking only medication therapy, in five patients after LF TENS , in three patients after HF TENS and in seven patients after cobination of HF and LF TENS. Slight Dysfunction was identified in two patients after medication therapy, in four patients after LF TENS , in three patients after HF TENS and in five patients after cobination of HF and LF TENS.



Dynamics of facial nerve dysfunction by House-Brackmann facial nerve grading system after treatment



High effective of LF TENS in left facial nerve neuropathy treatment (clinical case)

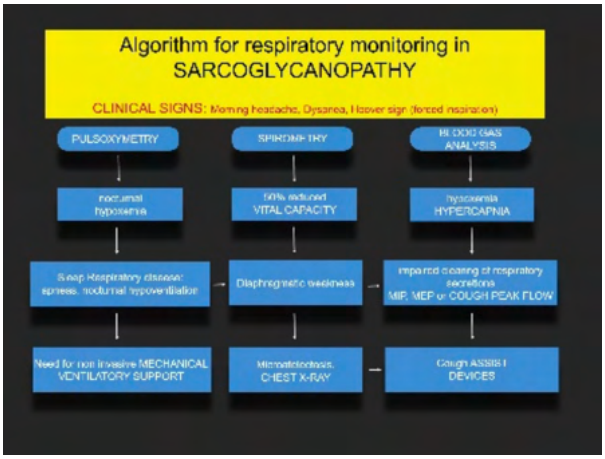
Conclusion: The use of TENS enhances the effect of drug therapy in the treatment of patients with neuropathy of the facial nerve. LF is more effective than HF in restoring motor function. At the same time, with a combination of LF and HF, the efficiency turned out to be significantly greater than when using exclusively LF.
Disclosure: Nothing to disclose.

EPO-147

An Algorythm to monitor respiratory insufficiency in sarcoglycanopathy

Corrado Angelini [1], Caterina Angelini [2]
[1] *Noventa Padovana, Italy,* [2] *Padova, Italy*

Background and aims: Sarcoglycanopathies (SG) are caused by mutation in SGCA, SGCB, SGCG or SGCD genes and present a wide spectrum of muscle involvement and wasting. The clinical phenotypes due to a mutation in the sarcoglycan genes include severe childhood-onset forms, proximal myopathies, pseudo-metabolic myopathies, myopathies with respiratory complication and hyperCKemia syndromes.covering the diagnosis and clinical respiratory care and cardiac complications of sarcoglycanopathies were reviewed in PubMed since the year 1997 and we choose to analyse those that covered series of patients.
Methods: The papers covering the diagnosis and clinical respiratory care and cardiac complications of sarcoglycanopathies were reviewed in PubMed since the year 1997 and we choose to analyse those that covered series of patients.
Results: Current diagnostic and therapeutic options linked to the management and monitoring of respiratory insufficiency present in 26% of cases, as well as physiotherapy/rehabilitation and drug treatment are considered and generated the proposed Algorhytm that should be used both in childhood and adult forms of sarcoglycanopathy.



Algorhytm to treat respiratory insufficiency in sarcoglycanopathy.

Conclusion: For optimal clinical care, both to offer effective management and to prevent and manage respiratory insufficiency. It is important both an early treatment and yearly monitoring with the proposed Algorhytm.
Disclosure: AFM grant 22392

EPO-148

Decoding neural responses to sounds in patients with disorders of consciousness

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[1] Liège, Belgium, [2] ExpORL, Neuroscience, Leuven, Belgium, [3] Department of Neurology, Liège, Belgium

Background and aims: In a clinical setting, residual cognitive functions of patients with disorders of consciousness (DOC) are assessed using behavioral and neuroimaging tools. However, confounding factors such as motor or hearing disabilities could interfere with the assessment and lead to misdiagnosis. This study aims to develop a novel objective and motor-independent diagnostic tool based on brain-computer interface technology and electroencephalography (BCI-EEG), integrating information about the patient's ability to hear, perceive, and understand instructions.
Methods: In this study, we will acquire data from 35 DOC patients. We will proceed in the following steps: (1) The auditory pathway's integrity will be assessed using evoked potentials paradigms (the auditory brainstem response and the auditory steady-state responses) to get information about the patient's ability to hear and perceive instructions. (2) We will evaluate the brain responses to a continuous, narrated story and measure the level of acoustic, phonetic, and semantic processing. (3) We will perform a BCI motor-independent task based on the auditory-attention detection paradigm; the patient will have to listen to two different stories simultaneously and focus on a specific one. (4) If the patient can follow the command, we will perform a yes-no question task with a-priori-known answers. For each question, the patient will answer 'yes' by focusing on one talker and 'no' by focusing on the other.
Results: This is a study protocol, results are not available.
Conclusion: With this study, we hope to understand auditory and speech processing better and find a new way to unlock communication in these patients unable to communicate verbally.
Disclosure: The authors have nothing to disclose.

EPO-149

Effects of low-frequency repetitive transcranial magnetic stimulation on motor recovery in early stroke patients

A. Gasnas
Chisinau, Moldova

Background and aims: The management of stroke patients in the acute period is extremely important for motor recovery, Unfortunately, there are currently no approved pharmacological agents that would help restore it. Transcranial magnetic stimulation (TMS) has been proposed to influence the altered motor function after stroke, but the results are still contradictory. We aimed to assess the TMS effectiveness in after-stroke early rehabilitation and to develop selection criteria for an ideal stroke candidate.
Methods: 95 subjects with acute ischemic stroke, in the territory of middle cerebral artery were selected and assessed through the following clinical scales: MMSE, Barthel disability scale, Orpington prognostic scale, mRS, NIHSS, MRC, 9-Hole-Peg Test (9-HPT) and the global clinical impression scale. A five days, inhibition TMS protocol 1 Hz, at 90% of the resting motor threshold, 10 sets, with an interval of five seconds (10 minutes, 600 pulses) was applied to 47 of them (randomly selected), after eliciting the motor evoked potentials (MEPs). (Fig. 1)

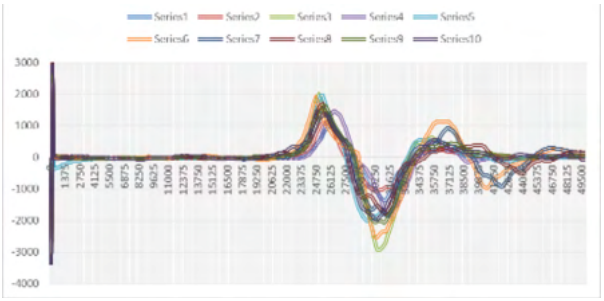

Figure 1. Example of an elicited motor evoked potential (MEP)

Results: The dynamics of the TMS group was statistically better compared to the control group according to all the applied scales ($p<0.05$), regardless of the topographic level, time from onset of stroke, age and sex. (Fig. 2, 3) The Spearman correlation confirmed that early MEP's absence is a negative predictor for the rehabilitation after stroke.

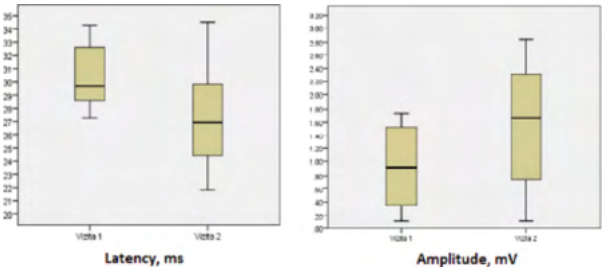

Figure 2. Dynamics of latency and amplitude of the motor evoked potential (experimental group), before and after TMS

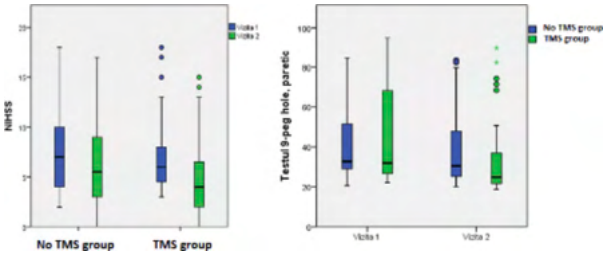

Figure 3. Dynamics of NIHSS score and 9-Peg-Hole test results in the paretic member (motor function) before and after TMS

Conclusion: The effect of TMS on cortical excitability confirmed its role in neurorehabilitation, compared to spontaneous recovery in the acute phase of stroke. We recommend the use of TMS in all subjects with ischemic stroke during the acute period.
Disclosure: Nothing to disclose.

EPO-150

A simple, low-cost, smartphone-based gait analysis. Preliminary results in healthy subjects

S. Gasparini [1], M. Lo Giudice [2], G. Varone [2], M. Ascoli [3], V. Cianci [4], G. Mastroianni [4], V. Dattola [4], C. Ieracitano [5], F. Morabito [5], E. Ferlazzo [6], U. Aguglia [4]
[1] Reggio Calabria, Italy, [2] Department of Medical and surgical sciences, Catanzaro, Italy, [3] Centro Regionale Epilessie, Reggio Calabria, Italy, [4] Neurology Unit Great Metropolitan Hospital, Reggio Calabria, Italy, [5] Dipartimento di Ingegneria Civile Elettrica dell'Ambiente e dei Materiali, Reggio Calabria, Italy, [6] Messina, Italy

Background and aims: Gait analysis is usually performed by mean of baropodometric examinations. We used a simplified, low-cost, smartphone-based gait analysis to encourage patients to constantly monitor gait and to report possible critical issues to the neurologist. We here present normative data from heathy subjects.
Methods: 50 healthy subjects were asked to wear a smartphone placed on the left wing, held by an elastic band, and to perform a standardized path. The free, open source, android "Phyphox" app acquired data from accelerometer during gait. The recorded data were transferred to a PC and elaborated in both Phyton and MATLAB languages. For each step, we extracted six features (min, max, mean, kurtosis, skewness and energy) of linear acceleration of the three axes (x=longitudinal, y=transversal, z=vertical) obtaining normative data from our sample.
Results: The following data were recorded: X-axis: min was -3.51 (SD±1.62), max was 4.90 (SD±2.34), mean was 0.12 (SD±0.32), kurtosis was 3.03 (SD±1.02), skewness was 0.40 (SD±0.65), energy was 14.86 (SD±5.27). Y-axis: min was -3.89 (SD ±1.95), max was 6.11 (SD±2.45), mean was 0.37 (SD ±0.36), kurtosis was 2.85 (SD±0.91), skewness was 0.41 (SD±0.53), energy was 18.21 (SD ±5.84). Z-axis: min was -5.07 (SD±1.62), max was 3.67 (SD ±2.36), mean was -0.20 (SD±0.32), kurtosis was 2.96 (SD ±1.02), skewness was -0.51 ± (SD±0.65), energy was 15.31 (SD ±5.27).
Conclusion: We provide normative results of smartphone-based, low cost gait analysis. Studies evaluating patients with neurological gait disturbances are ongoing.
Disclosure: Nothing to disclose.

EPO-151

Does movement affect cognitive function in patients after a stroke?

P. Konečný [1], J. Vyskotova [2], P. Gaul Alacova [2], A. Muckova [2], M. Vorlicek [3], M. Roubec [4], D. Školoudík [5]
[1] Olomouc, Czech Republic, [2] Clinical Rehabilitation, Faculty of Health Sciences, Palacký University Olomouc, Olomouc, Czech Republic, [3] Faculty of Physical Culture, Palacký University Olomouc, Czech Republic, Olomouc, Czech Republic, [4] Faculty of Health Sciences, Palacký University Olomouc, Czech Republic, Olomouc, Czech Republic, [5] Department of Neurology, Ostrava, Czech Republic

Background and aims: Cognitive impairment is one of the most common diseases in the population. Cognitive functions can be influenced by a large number of interventions – for example physical aktivity, cognitive rehabilitation, pharmacotherapy.
Methods: Evaluation of the effect of walking movement therapy on cognitive function in patients after stroke. The partial goal was to evaluate the effect of exercise therapy on the change in self-sufficiency during daily activities and the change inthe value ofthe Body Mass Index. Methodology: 40 patients after stroke were followed for one month. The Garmin Vivofit 3 smart watch was used th recorda monthly movement intervention (number of steps). The MoCA test (Montreal Cognitive Test), BI (Barthel Index) score and BMI (Body Mass Index) evaluated the effects of movement intrevention. Tests values were measuredat the begining and the end (after one month) of the intevention. The measurement results were statistically processed and evaluated (ANOVA).
Results: There is a significant correlation between the number of walking steps and the change in cognitive functions according th the Spearman correlation test (r=0.4; p=0.007). Another result of the study is a significant change in BMI after one of month of walking therapy (p=0.024). The cut-off value for significant changes in cognitive function and BMI is 6,000 steps per day. Changes in self-sufficiency during daily activities after one of month of walking therapy is not significant.
Conclusion: Walking has the positive effect on improving cognitive function and the change in the Body Mass Index. The walking should be included in the daily physical regime.
Disclosure: This study was supported by The Junior Grant of Palacký University Olomouc (No. JG_2019_004: The influence of atherosclerosis on the development of dementia and the possibility of its non-pharmacological influence).

EPO-152

MBP as a predictor of neurological recovery in patients with acute ischemic stroke during early rehabilitation

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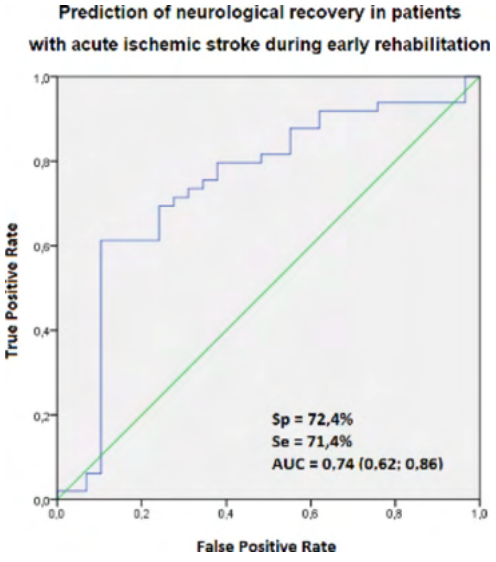
Background and aims: Myelin basic protein (MBP) is attaching myelin sheath to oligodendrocytes, involved in signaling and is increasing in acute ischemic stroke (AIS). The Hypothesis: evaluation of serum MBP on day two of AIS and assessment by FMA score as an indicator of corticospinal tract preservation are suitable for individual prediction of sensorimotor recovery during early rehabilitation (first 14 days).
Methods: Statistical modeling was performed using Linear discriminant analysis. Training sample included data of 78 patients on day two of AIS: middle age 61(57;65) years, NIHSS=8(5;12), FMA=167(133;189) points. The concentration of serum MBP was determined by using DY4228-05 Human MBP DuoSet ELISA-kit (R&D Systems, USA). System thrombolysis or thrombectomy was not carried out.
Results: Clinical improvement (increase in NIHSS by two or more points) was registered in 49 patients, without improvement – in 29. Discriminant prediction model was statistically significant (F=17, p<0.001), specificities of 72,4%, sensitivities of 71,4% (Figure 1). Standardized coefficients of canonical linear discriminant function (QLDF), reflecting the " weight" of variable in the model, were for FMA 1,084, for MBP 0,556. The cut-off point is defined as midpoint of distance defined between the centroids of the classes and is equal 0,6299. Decisive rule of the model:QLDF=-7.938+0.045*FMA+0.033*MBP.



Quality of a binary classifier based on a discriminant model

Conclusion: Quantitative features of serum MBP and assessment by FMA on the second day of AIS allows to build an individual prediction of sensorimotor recovery in the first 14 days. Statistical model is solving topical issues of dosage, safety, effectiveness of early rehabilitation, is providing the choice of competent treatment and rehabilitation tactics.
Disclosure: Nothing to disclose.

EPO-153

The effectiveness of training with exoskeleton for restoring gait in the early recovery period of stroke

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K. Petrushanskaya [1], E. Pismennaya [1], L. Kodzokova [1]
[1] *Department of Neurology, Moscow, Russian Federation,*
[2] *Russian Federation*

Background and aims: Impaired locomotor function is one of the most severe consequences of stroke, disrupting daily activity and reducing the quality of life of patients. Aim of study - to evaluate the effectiveness of restoring walking function in patients in the early recovery period of ischemic stroke (IS) using an exoskeleton.
Methods: The study included 49 patients (average age-63.4±11.2 years), 1–3 months after IS (2.6±1.1 months). In group 1 (n=23), trainings with exoskeleton were used in the complex of rehabilitation treatment, patients in group 2 (n=26) received a standard rehabilitation course. Neurological deficit was assessed before and after treatment on the Medical Research Council Scale, modified Ashworth scale, Berg balance scale, Hauser Walking index, 10-meter walking test, Rankin scale, Barthel index. For objectification, stabilometry and biomechanics of walking were used.
Results: There was a statistically significant improvement in walking quality (median 1.0 [0.0;1.0] points and 0.0 [0.0;0.0] points, respectively ($p<0.01$) and walking speed (3.7±1.5 sec. and 2.4±1.3 sec. accordingly ($p<0.05$) in group 1 when using an exoskeleton compared to group 2. There was an improvement in balance (median 7.5 [5.0; 8.3] points and 4.6 [4.6;5.0] points, respectively ($p<0.01$) and a decrease in the energy consumption index for maintaining a vertical posture (6.2±6.1 J and 1.1±1.8 J, respectively ($p<0.001$) in patients of group 1 compared to group 2.

Indicators	1 group			2 group		
	Day 0	Day 14	Dynamics	Day 0	Day 14	Dynamics
MRCS, Me [Q1;Q3]	4,0 [3,0, 4,0][B]	5,0 [4,0, 5,0][A]	1,0 [0,0, 1,0] [D]	4,0 [3,0, 4,0]	4,0 [4,0, 4,0] [C]	0,0 [0,0, 1,0]
MAS, Me [Q1;Q3]	4,0 [2,0, 4,0][B]	3,0 [2,0, 4,0][E]	0,0 [0,0, 0,0] [D]	3,0 [3,0, 4,0]	3,0 [3,0, 3,0] [D]	0,0 [0,0, 0,0]
BBS, Me [Q1;Q3]	41,0 [40,8, 46,0][B]	46,0 [44,8, 56,0][A]	7,5 [5,0, 8,3][F]	41,0 [41,0, 45,25]	45,6 [45,6, 50,3][A]	4,6 [4,6, 5,0]
HAI Me [Q1;Q3]	4,0 [4,0, 5,0][B]	5,0 [3,0, 4,0][A]	1,0 [0,0, 1,0][F]	4,0 [4,0, 5,0]	4,0 [4,0, 4,0] [D]	0,0 [0,0, 0,0]
10MWT M±SD	21,3±3,1[B]	17,5±4,0[A]	3,7±1,5[G]	21,7±3,6	19,3 ±4,6[A]	2,4±1,3

MRCS - Medical Research Council Scale, MAS - Modified Ashworth Scale, BBS - Berg Balance Scale, HAI - Hauser Ambulation Index, 10MWT - 10 meter walking test. A – $p<0,001$ between Day 0 and Day 14, B – $p<0,01$ between Day 0 and Day 14, C – $p<0,05$ between Day 0 and Day 14, D – $p<0,05$ between Day 0 and Day 14, E – $p<0,001$ between groups 1 and 2, F – $p<0,01$ between groups 1 and 2, G – $p<0,05$ between groups 1 and 2, H – $p<0,05$ between groups 1 and 2.

Indicators of muscle strength, spasticity, balance, walking function, walking speed of patients of groups 1 and 2 before and after rehabilitation.

Conclusion: There was revealed the positive effect of exoskeleton training on the restoring locomotor function and dynamic parameters of walking in patients in the recovery period of IS with the inclusion of exercises with an exoskeleton.
Disclosure: There is no conflict of interest.

EPO-154

Evaluation of motor rehabilitation and neuroplasticity using transcranial magnetic stimulation after ischemic stroke

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[1] Tomsk, Russian Federation, [2] Research Institute of Balneology, Tomsk, Russian Federation

Background and aims: Repetitive transcranial magnetic stimulation (rTMS) is one of the perspective methods of non-invasive brain stimulation that activates brain neuroplasticity. **Aim:** to evaluate the effect of repetitive transcranial magnetic stimulation on the degree of motor deficit and the level of biological markers of brain neuroplasticity in patients after ischemic stroke in the early recovery period.
Methods: The study involved 63 patients with ischemic stroke (average age 67(58–71) years; Rankin scale 4(4–5); NIHSS=9(8–13) moved to the 2nd stage of rehabilitation in Research Institute of Balneology. The course of motor rehabilitation was 20 days. Two groups of patients: One group (32 patients) received traditional rehabilitation program; two group (31 patients) additionally received high-frequency (> HZ) rTMS on the affected part of the hemisphere. Neurological examination was completed by Fugl-Meier Assessment (FMA). BDNF was determined by MAGPIX multiplex analyzer (Luminex, USA) using xMAP® Technology.
Results: One group: FMA I=134 (129–143); FMA II=146(138–159); p=0,05 BDNF I=1,332(992–1,562)pg/ml; BDNF II=1207(1,057–1,721)pg/ml; p=0,53 two group: FMA I=148(132–156); FMA III= 172(158–181); p= 0,04 BDNF I=734(702–779)pg/ml; BDNF III=1,644(1,592–1,698)pg/ml; p=0,02 Strong positive correlation was found after rehabilitation with rTMS between BDNF and FMA (r=0,74; p=0,05) as opposed to the traditional therapy group (r=0,32; p=0,09)
Conclusion: rTMS has established itself as an effective method of rehabilitation that stimulates the neuroplasticity of the brain. It is recommended to add rTMS to the traditional rehabilitation program.
Disclosure: Nothing to disclose.

EPO-155

The impact of the cortical silent period at transcranial magnetic stimulation in rehabilitation after stroke

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Background and aims: The purpose of this study was the study and assessment of neurophysiological value of contra- and ipsilateral cortical silent period (cSP) in the dynamics of rehabilitation of patients after stroke at therapy of TMS.
Methods: A randomized, single-blind, placebo-controlled study was conducted in 102 patients with cerebral stroke in three groups. In the first group (40 patients), high-frequency repetitive TMS (rTMS) of the motor zones of the affected hemisphere was performed; the second group (41 patients) underwent multilevel magnetic stimulation (MS), the third group (21) – placebo-TMS (sham TMS).
Results: CSP and TI were recorded in 65 patients, of which in nine they were not recorded from both hemispheres.In patients with right-sided stroke in the initial state, there was an increase in the contralateral cSP ($p<0.01$) in comparison with the control (Tab.1). TI in right-sided stroke on the affected side is increased relative to the control ($p<0.01$). After a course of TMS therapy, in the first[t] and second group there is a positive dynamics of cSP and TI from both hemispheres (Table 2). In the first group, there was a decrease in TI, in the second and third without changes (Table 3).

Stimulation	Silence period, ms				
	Affected side		The intact side		The control
	right	left	right	left	
CONTRA	197,9±32,8**	150,0±17,6	144,8±11,8	142,1±12,9	127.9±2.8
IPSI	46,4±6,3**	25,8±3,6	26,3±2,8	27,6±2,8	26.9±3.8

Note: * - reliability of the difference, calculated in relation to the initial state; * - p <0.05; ** - p <0.01

Table 1. The results of contra- and ipsilateral cSP

Therapeutic groups	Cortical Silence Period, ms	
	before	after
I group	178.0 ± 14.8 * / 134.1 ± 11.0	149.7 ± 10.6 / 134.5 ± 11.7
II group	181.5 ± 19.6 * / 170.0 ± 27.3	242.1 ± 57.3 / 148.9 ± 18.4
III group	175.7 ± 47.6 / 133.4 ± 16.8	175.5 ± 48.9 / 127.6 ± 11.3

Note: in the numerator - indicators from the affected side, in the denominator - indicators from the intact side; * - the reliability of the difference, calculated in relation to the initial state, * - p <0.05

Table 2 Cortical Silent Period in therapeutic groups

Indicators	Therapeutic groups	I group	II group	III group
SILENCES PERIOD, ms	before	30,7 ± 3,9 24,5 ± 1,6	43,7 ± 18,9 34,3 ± 10,8	43,0 ± 9,7 29,6 ± 4,6
	after	30,8 ± 4,5 26,1 ± 1,3	38,3 ± 6,5 17,5 ± 2,7	18,8 ± 14,7 25,6 ± 2,2
THE CONTROL		26,9 ± 5,8		

Table 3 Comparative indicators of TI duration relative to reference values

Conclusion: The impact of the contralateral cSP from the affected hemisphere underwent changes to a greater extent after the rTMS course than the indices of the ipsilateral cSP. In the second treatment group, on the contrary, the duration of cSP from the affected hemisphere increased.
Disclosure: Nothing to disclose.

EPO-156

Safety and efficacy of vortioxetine on depressive symptoms and cognition in post-stroke patients: a pilot study

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Background and aims: Post-stroke depression (PSD) is the most frequent complication in subacute stroke survivors. No studies have examined safety and efficacy of vortioxetine on PSD. The aim is to evaluate the safety and the efficacy of vortioxetine on PSD in subacute stroke survivors.
Methods: All consecutive patients admitted to EPO112 Neurorehabilitation Department after ischaemic or haemorrhagic stroke from the July 2018 to July 2020 (Group1) were prospectively evaluated for depressive symptoms (BDI-II) and cognitive function (MoCA). All subjects with relevant depressive symptoms (BDI-II score21) were treated with vortioxetine (orally administered once daily at 5mg for seven days, then increased to 10mg for the three weeks). Safety of vortioxetine and its effects on PSD and cognition was evaluated after eight weeks of treatment by a blind rater (t0–t1). Adverse events and side effects were collected.
Results: Out of 176, in Group1 (21 patients; mean age (SD): 77(33)years) BDI-II mean score decreased from 24(t0) to 8(t1); MoCA mean raw score increased significantly from 16(t0) to 19(t1). Out of 166 patients admitted from April 2017 to April 2018, 10 (Group2) aged 70.5(26) years, treated for the first[t] time withSSRI-SNRI/NSSA was matched for age, sex, Barthel Index, BDI-II and MoCA with Group1 using Mann-Whitney U-test and Chi-squared Test. In both groups BDI-II score decreased at t1, without a concomitant increase in MoCA scores. Comparing Group1 and Group2,delta-BDI-II does not varies, while delta-MoCA significantly increase. No adverse events and side effects were recorded.
Conclusion: Vortioxetine appears to be safe and showing effect on PSD and cognition.
Disclosure: Nothing to disclose.

EPO-157

The main patterns of neurological symptoms in patients with chronic disoders of consciousness

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Background and aims: Treatment and rehabilitation of DOC patients affects not only medical, but also social and ethical aspects.
Methods: 324 DOC patients – 291 patients in the vegetative state/unresponsive wakefulness syndrome VS/UWS (184 men) and 33 patients in minimally conscious state MCS "plus" (20 men). Age ranged from 16 to 71 years (mean age 31). The average duration of disorders of consciousness at the time of admission to the department was 4.4±0.7 months.
Results: Depending on the prevalence of neurological symptoms, VS/UWS patients were divided into four main clinical patterns. The main characteristics of the I VS/UWS clinical pattern were considered as: duration of spontaneous wakefulness periods less than 1/3 of the daytime or eyes opening only for stimulation; decrease or absence of spontaneous involuntary (reflex) activity; a decrease in muscle tone. The second pattern was distinguished by the presence of hyperkinesis: single or multiple myoclonia, dystonia, hemiballism. The third pattern was characterized by stereotypical reactions in the form of the appearance of a grimace of pain, discontent, crying to any external stimulation (touch, verbal command); patients without a tracheostomy cannula made loud " moo " sounds, moans, without distinct verbalization. The IV pattern was represented by an increase muscle tone (extrapyramidal type), as well as catatonia, tremor, hypomimia, etc.
Conclusion: The best outcome was observed in the forth pattern, and the worst results were observed in the third clinical pattern.
Disclosure: The study is supported by the grant of the RFFR 19-29-01066.

Peripheral nerve disorders

EPO-158

Case study: Gly53Ala transthyretin amyloidosis with small fibre sensory and autonomic neuropathy and cardiac involvement

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Background and aims: Hereditary transthyretin amyloidosis (hATTR) is a rare disease characterised by transthyretin amyloid deposition in the extracellular tissue. This deposition causes multisystem dysfunction, notably sensorimotor and autonomic neuropathy and cardiomyopathy. Previously, a Gly53Ala (p.Gly73Ala) variant has been described with leptomeningeal amyloidosis in a British case study. We present the second incident of this variant, with a novel phenotypic description.
Methods: The patient was phenotypically mapped based on medical history, clinical examination and measures for 1) neurogenic autonomic dysfunction, 2) small and large fibre polyneuropathy, 3) central nervous system involvement and 4) cardiac involvement.
Results: The 39-year-old male patient presented with pain and allodynia in the feet, erectile dysfunction and orthostatic intolerance. The clinical examination showed pure small fibre polyneuropathy with reduced cold and pinprick sensations in the feet, reduced sweat volume measured by quantitative sudomotor axon reflex testing and reduced intraepidermal nerve fibre density in the lower leg. The electroneuronography was normal. Cardiovagal dysfunction was present with reduced heart rate variability to deep respiration and Valsalva manoeuver. Cardiovascular adrenergic function was unimpaired with normal blood pressure responses to Valsalva-manoeuver and tilt-table testing. DPD scintigraphy was positive with Perugini grade III. Echocardiography demonstrated normal ejection fraction and global longitudinal strain but discrete concentric hypertrophy. Transthyretin amyloid deposition was identified, initially in fat aspirate by immuno-histochemistry, later in an endomyocardial biopsy by Congo red staining suggesting active disease. MRI with contrast did not show leptomeningeal amyloid deposits.
Conclusion: The patient had a mixed hATTR phenotype with cardiac involvement and small fibre sensory and autonomic polyneuropathy.
Disclosure: Funding from Lundbeckfonden.

EPO-159

Guillain-Barré Syndrome during pregnancy: case series

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Background and aims: Guillain-Barré syndrome (GBS) in pregnancy is a rare condition. It may be a serious disease associated with high maternal and perinatal morbidity and mortality. The aim of our study was to identify all pregnant women in a cohort of GBS female patients of germ age from our center and to retrospectively analyze long-term maternal and fetal outcomes.
Methods: Our study included five GBS pregnant patients diagnosed from January 2007 to June 2019 in one health center. Sociodemographic and clinical data were obtained from the medical records. Functional disability was assessed by the Guillain-Barré syndrome disability scale (GDS). Patients and their babies were followed for one year.
Results: The mean age of pregnant GBS patients were 29.8 ± 3.1.Two patients (40%) had severe disability at admission (GDS>3). Three patients (60%) were treated with intravenous immunoglobulins, while remaining two (40%) were treated symptomatically. Only one patient was severely disabled on discharge (GDS 4). One year after disease onset, one patient (20%) had mild disability (GDS 2), while remaining four had normal neurological findings. All patients who delivered had healthy babies and during follow-up, all babies had normal development.
Conclusion: GBS during pregnancy is a rare condition with generally good outcomes for both mother and fetus. The treatment options are the same as for non-pregnant patients. One year after the onset of the disease, up to 20% of mothers may have a certain degree of disability.
Disclosure: Nothing to disclose.

EPO-160

Sensorymotor neuropathy with dysautonomia associated to SORD gene mutations

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Background and aims: Hereditary neuropathies (HN) are a clinical and genetically heterogeneous group of peripheral nerve disorders. Distal motor HN have predominant motor features. New genetic sequencing techniques have been relevant in the molecular diagnosis of these pathologies.
Methods: Case report
Results: 17-year-old girl with progressive lower limb (LL) weakness, pain, local temperature and trophic changes. Complaints were asymmetric (mainly right) and were preceded by distal paresthesias since 11yo. Remaining pathological and family history were unremarkable (parents not consanguineous). Her neurological examination revealed moderate feet wasting and LL livedo. Weakness was present and symmetric in hands – finger abduction and extension (G4+) – but was more significant in her feet – plantar flexion (G3), dorsal flexion (G2) and hallux extension (G1/2). Ankle reflexes were absent, and the sensation was also changed in LL: distal hypopalesthesia and hypoesthesia in a high-stocking distribution. She was unstable with eyes closed. She had a bilateral steppage gait and was incapable of walk in her toes or heels. Sensory and motor nerve conduction studies revealed chronic peripheral motor nerve lesion in her LL compatible with axonal motor neuropathy. Complementary examination with unremarkable results included medullary MRI, blood analysis with systemic autoimmunity, alpha-galactosidase and next-generation-sequencing for distal muscle atrophies. Clinical exome sequencing revealed a SORD gene homozygotic change [c.757del (p.(Ala253Glnfs*27))], associated to sorbitol dehydrogenase deficiency.
Conclusion: SORD mutation-associated neuropathy was first described in 2020 and is a predominantly motor neuropathy. However, sensory complaints and local dysautonomia can be major features that should not preclude the study of this mutation.
Disclosure: Nothing to disclose.

EPO-161

Demyelinating polyradiculoneuropathy in patients with metastatic melanoma treated with nivolumab: report of two cases

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Background and aims: Nivolumab, an anti-PD1 antibody, belongs to the checkpoint inhibitors used for treatment of metastatic melanoma, by increasing the immune response to cancer. However, this intensified immune response may result in immune-mediated adverse events. We describe the cases of two patients treated with nivolumab, which developed demyelinating polyradiculoneuropathy.
Methods: Cases reports
Results: Case 1: A 76-year-old man, diagnosed with malignant melanoma in 2015, with bone progression in 2020, received treatment with nivolumab and relatlimab (anti–LAG3). After three months of treatment, the patients developed muscle weakness in lower extremities and paraesthesia in fingers and toes. Physical examination showed tetraparesis 4/5 with areflexia. The lumbar puncture showed albuminocytological dissociation. The MR of spinal cord was normal. The neurophysiological study showed a sensory-motor demyelinating polyradiculo-neuropathy with conduction blocks, with a slight associated axonal component. After treatment with intravenous immunoglobulin and corticosteroids and discontinuation of nivolumab, the symptoms improved. Case 2: A 59 year-old woman, diagnosed with melanoma in 2011, with metastatic progression in 2020, received treatment with nivolumab. After three month of treatment, the patient developed muscle weakness in lower extremities. The lumbar puncture showed albuminocytological dissociation. The neurophysiological study showed a sensory-motor demyelinating polyradiculoneuropathy with conduction blocks. Onconeuronal antibodies were negative. After treatment with oral corticosteroids and discontinuation of nivolumab, muscle weakness improved.
Conclusion: These cases highlight the association between nivolumab and immune-mediated peripheral polyradiculo-neuropathy as a neurologic immune-related adverse of immune checkpoint inhibitors. Physicians should be aware of that association in order to diagnose it and treated it as soon as possible.

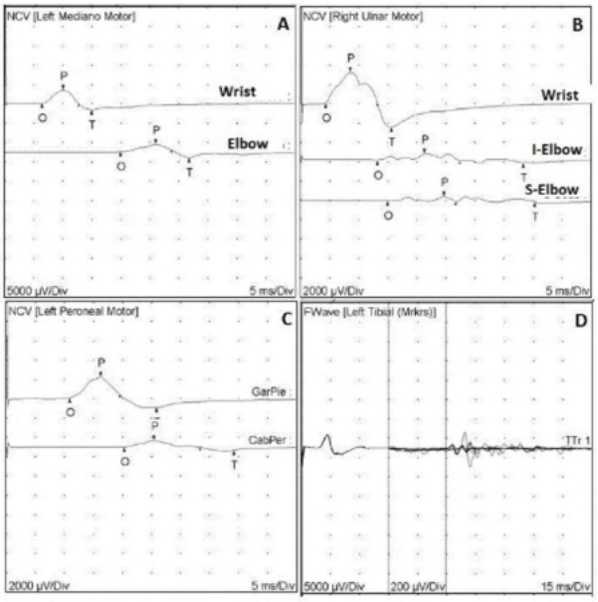

Figure 1. Electroneurography findings: Conduction blocks in motor nerve of upper limbs (A, B) and lower limbs (C) with prolonged F-wave latencies in nerves with a normal compound muscle action potential amplitude (D).

Disclosure: Nothing to disclose.

EPO-162

Characterization of dysautonomic symptoms in Guillain-Barré Syndrome

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Background and aims: Dysautonomic symptoms (DS) are a major cause of mortality in Guillain-Barré syndrome (GBS), along with weakness of the respiratory and bulbar muscles. We aimed to characterize DS in patients diagnosed with GBS.

Methods: A retrospective review of patients admitted to Hospital Egas Moniz between January 2010 and June 2020 with the diagnosis of GBS. Clinical, neurophysiological and laboratory data were collected. DS were defined as the presence of at least one of the following: hyper/hypotension, tachy/bradycardia, urinary retention, ileus, sudomotor dysfunction, hyper/hypothermia. GBS disability scale, mEGOS and EGRIS were calculated for each patient. Logistic regression was performed to evaluate potential predictors of DS.

Results: 45 patients with GBS were included, 64.4% male, with a mean age of 55.9 years. The most frequent DS was tachycardia (69%), followed by hypertension (62.1%), ileus (62.1%), urinary retention (44.8%), hypotension (31%), bradycardia (24.1%), sudomotor dysfunction (13.8%) and hyperthermia (10.3%). Most DS-GBS patients presented the demyelinating subtype (75.9%). DS-GBS patients had longer hospital stays, higher CSF protein and heart rate variability; and worst scores on the GBS disability scale, mEGOS and EGRIS ($p<0.05$). The logistic regression model showed that only GBS disability scale was a predictor of DS ($p=0.026$, OR 0.076, CI95% 0.008–0.732).

Conclusion: DS are frequent in GBS, occurring in 2/3 of our patients, although tachycardia, hypertension, ileus and urinary retention were superior in our study when compared with the literature. The DS-GBS patients had a longer hospital stay and a more severe disease. GBS disability scale was the best predictor of DS in our patients.

Disclosure: Nothing to disclose.

EPO-163

Biomarkers of diabetic foot syndrome

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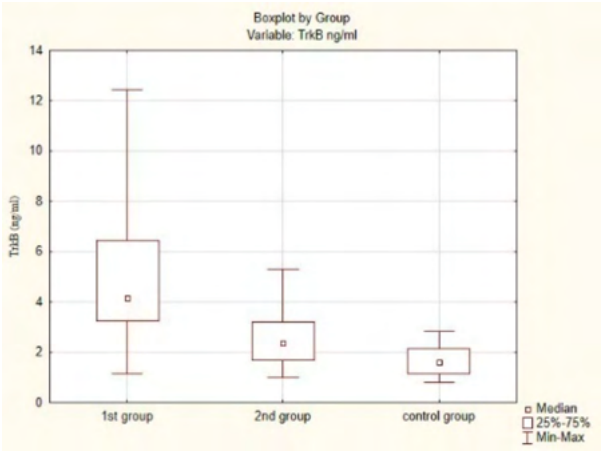
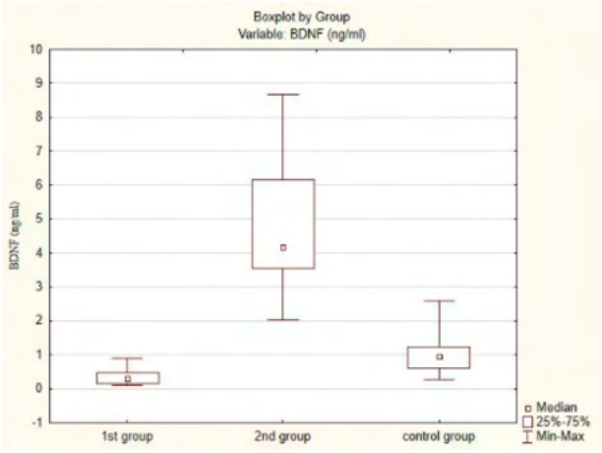
Background and aims: Laboratory studies of neurotrophic factors and their specific receptors can play an important role in an early diagnosis of diabetic foot syndrome (DFS). Aim of research was to study a prognostic significance of brain derived neurotrophic factor (BDNF) and tropomyosin receptor kinase type B (TrkB) in development of DFS.
Methods: 48 patients with diabetic polyneuropathy (DPN) were examined by standard neurological examination and electroneuromyography (ENMG) with measuring nerve conduction velocity, amplitude and latency of peroneal nerve. All patients were divided into two groups: the first group consisted of 20 patients with severe DPN, associated with DFS; 28 patients with moderate DPN were included in the second group. Control group consisted of 14 healthy persons. Serum contents of BDNF and TrkB were measured by enzyme immunoassay.
Results: The first group was characterized by more pronounced objective clinical signs and ENMG-parameters of DPN (table 1). Patients of first group had the highest serum level of TrkB (4.35±1.03ng/ml) versus patients of second group (2.55±1.27ng/ml, p=0.001) and control group (1.66±0.62ng/ml, p=0.000). The average serum BDNF in first group was 0.34±0.22ng/ml, which was statistically less than the corresponding level of second group (4.69±2.01ng/ml, p=0.001) and control group (1.06±0.64 ng/ml). There were revealed correlations between the increase serum TrkB and the severity of neuropathy by low nerve conduction velocity (r=-0.492, p=0.000) and the increase latency of peroneal nerve (r=0.366, p=0.001).

Parameters	Group 1	Group 2	U-test	P-value
Age, years	57,50±14,78	59,22±8,75	0,882	0,377
Duration of DM, years	15,2±8,10	13,27±8,39	0,753	0,223
Fasting blood glucose level, mmol/l	12,77±3,64	9,58±2,84	1,644	0,519
HbA1c, %	9,85±1,91	7,56±2,04	2,678	0,007*
Neuropathy disability score	16,85±6,58	13,29±5,83	0,862	0,012*
M-amplitude, mV	1,01±0,91	2,23±1,57	-2,282	0,001*
Latency M-amplitude, mc	4,85±1,97	3,22±1,3	1,965	0,019*
Nerve conduction velocity, n.peroneus, m/s	23,17±9,47	35,33±5,95	-1,162	0,000*

Clinical and neurophysiological parameters of studied groups



Average levels of TrkB in studied groups



Average levels of BDNF in studied groups

Conclusion: The high expression TrkB and low level of BDNF in serum may be considered as laboratory predictors of a diabetic foot syndrome.
Disclosure: The authors declare no conflict of interest.

EPO-164

Timescales in chronic inflammatory demyelinating polyneuropathy diagnosis

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Background and aims: Chronic inflammatory demyelinating polyneuropathy (CIDP) is an immune-mediated disease of peripheral nervous system with progressive or relapse-remitting course. The diagnosis of CIDP reveals on clinical presentation and electrophysiological data due to EFNS/PNS criteria.
Methods: The aim of this study was to determine approximate time which is needed to make a CIDP diagnosis and time needed for a patient to make an appointment to general practitioner after first symptoms of CIDP appeared. 112 patients with confirmed CIDP diagnosis were investigated at inpatient department: 66 males and 46 females; 21 patients with diabetes mellitus (DM) and 91 without. Clinical and laboratory assessment were performed to all patients.
Results: The average time between earliest symptoms and CIDP diagnosis was 2,64±0,38 years and average time between earliest symptoms and visit to general practitioner was 0,4±0,08 years. Assessed comparison groups included different gender, age, presence of DM, normal and elevated laboratory parameters and degree of neurological deficit. Groups with statistically significant differences presented in Table 1. Time from symptoms to doctor's appointment did not depend on assessed factors. Differences between different age groups, levels of neurological deficit and other laboratory results were not found.

	Time between earliest symptoms and diagnosis	Significance, p
Males	3,31±0,58	p<0,05
Females	1,68±0,34	
Patients with DM	1,33±0,49	p<0,05
Patients without DM	2,94±0,44	
Elevated creatine kinase level (>200 U/l)	3,71±1,29	p<0,05
Normal creatine kinase level (<200 U/l)	1,97±0,46	

Table 1. Time between earliest symptoms and CIDP diagnosis in different groups

Conclusion: Diagnosis of CIDP is a challenging approach, which consumes a lot of time in comparison to many other neurological diseases. DM affects the course of CIDP and possibly it takes less time to diagnose CIDP due to higher neurological deficit. Earlier diagnosis in women can be explained by their higher adherence to doctor's prescriptions. But the effect of creatine kinase level on timescales remains unclear.
Disclosure: Nothing to disclose.

EPO-165

Quantitative proteomic analysis of cerebrospinal fluid from patients with facial nerve palsy

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Background and aims: Bell's palsy (BP) is the most common form of peripheral facial paralysis (FP), accounting for over 60% of cases. BP is assumed to be caused by nerve swelling due to inflammation and/or viral infection. Functional and structural alterations of nervous tissue can be reflected in the protein composition of the cerebrospinal fluid (CSF). We therefore applied an integrative proteomic approach to identify possibly altered protein expression patterns in the CSF of BP patients.
Methods: CSF samples were obtained from 29 patients suffering from FP, including 17 with BP, four with varicella zoster virus-associated FP (VZV-FP), and eight with FP of unknown etiology (normal CSF cell counts, but elevated CSF protein (FP-EP)). Five patients with headache who were punctured to exclude secondary headache served as controls. The samples were subjected to liquid chromatography tandem mass spectrometry and bioinformatics analysis, multiplex cytokine/chemokine arrays, and Biofire® filmarrays (meningitis/encephalitis panel).
Results: All samples, except those from VZV-FP patients, revealed a negative Biofire® test. The protein composition of CSF samples from BP patients was comparable to that of controls. An array of dysregulated proteins was identified in CSF samples from VZV-FP and FP-EP patients compared to controls. The CSF proteome in FP-EP patients was similar to that of VZV-FP patients. The identified dysregulated proteins were involved in pathways for complement activation, cell signaling and adhesion. Multiplex analyses revealed elevated cytokine/chemokine levels in the CSF of FP-EP and VZV-FP, but not BP patients.
Conclusion: Our study revealed no evidence for a viral or inflammatory cause of BP.
Disclosure: The authors declare no conflict ofinterest.

EPO-166

Evidence of post-COVID-19 polyneuropathy

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Background and aims: It was shown that SARS-Cov2 affects not only the central nervous system, but also the peripheral. Cases of Guillain-Barré syndrome and plexopathy induced by the virus are described. But, surprisingly, we found only a few reports on the development of chronic polyneuropathy. We want to present our observation of post-COVID-19 complication in the form of slowly progressive polyneuropathy.
Methods: We observed 12 patients (mean age 46±11.3, men (7) women (5). All patients had mild to moderate COVID-19 infection. None of the patients received a drug with a probable toxic effect on peripheral nerves. Electroneuromyography was done in all cases.
Results: Mean time of onset of clinical symptoms was 24±16.5 days after the end of acute episode of COVID-19. All patients had predominantly axonal damage of the peripheral nerves (only the sensory fibers – in 10 cases, sensory and motor fibers – in two cases. No cases of paresis were detected. The period of observation of the patients was up to five months. No case of complete recovery was observed. Three patients had progression of sensory impairments as well as symptoms of axonopathy.
Conclusion: In our opinion, not enough attention is paid to this problem. Considering the onset of symptoms in post-COVID-19 period (after recovery), we can think about an immune-mediated pathogenesis of peripheral nerves damage. In general, post-COVID-19 polyneuropathy is characterized by sensory impairment and axonal damage on electrophysiological examination.
Disclosure: No conflict of interest.

EPO-167

Outcomes of nerves transfers for motor recovery of hand function in brachial plexus injury: A systematic review

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Background and aims: Complete traumatic brachial plexus injury causes complete dysfunction of motor hand functions, which represents a challenge for the neurosurgeons. To date, many techniques have been developed to reinnervate the hand of patients with a total brachial plexus injury. This systematic review describe the outcomes of hand reinnervation in brachial plexus injury in adults.
Methods: The search strategy used the medical subject headings (MeSH) and text words related to "brachial plexus injury" and "hand". The databases included were PubMed and BVS. Following PRISMA guidelines, 713 studies were identified and 11 were included. The NOS scale were utilized for assess the quality of the studies selected.
Results: Of the studies analysed, the transfer of the phrenic nerve to the posterior division of the lower trunk revealed an average of 75% of patients with an M3 in The British Medical Research Council (MRC). The patients who obtained the transfer of the contralateral root of the C7 nerve, 74.5% showed paraesthesia of the thumb in three months postoperatively in one study, and 97% showed temporary paraesthesia of the median nerve after surgery in another study. The neurotization of four intercostal nerves and the use of C5 root graft, only 19% of patient patients improved at least 24 months postoperatively, while 70% of patients achieved finger flexion assessed at a maximum of M3, on average 77, 5 months postoperatively.
Conclusion: We observed negative outcomes in patients undergoing surgical techniques for hand reinnervation, requiring the development of new techniques that ensure a best prognostic for the patients.
Disclosure: Yes

EPO-168

Hyperglycemia and clinical outcome of Guillain-Barré syndrome

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Background and aims: Elevated blood glucose is common in different neurological diseases as stroke, usually with worsening of the clinical outcome. An association between Guillain-Barré syndrome (GBS) and blood glucose level has been studied very rarely. The aim of this study was to analyze if hyperglycemia at the admission may influence the severity of GBS including mechanically ventilated patients.

Methods: We retrospectively studied 73 patients, who fulfilled the clinical criteria for diagnosis of GBS. Seven patients (9.6 %) suffering from diabetes mellitus were excluded and the final analysis was proceeded in 66 patients (40 males, 19–93 years, average 56 years) free of corticoid treatment. Hyperglycemia (the level of fasting plasma glucose, FPG) was defined as blood glucose level >5.59 mmol/L according to our laboratory.

Results: At admission, 32 GBS patients (48%) had hyperglycemia according to FPG level. Severe form of GBS (>4 due to Hughes GBS scale) was observed in 17 patients (26%); and eight of them (47%) had hyperglycemia. 14 patients (21%) were mechanically ventilated and in 10 of them (71%) hyperglycemia was present.

Conclusion: Our data suggest that hyperglycemia in the acute phase of GBS is not rare and may influence the severity of GBS symptoms. Stress hyperglycemia may be the explanation for impaired glucose homeostasis.

Disclosure: Nothing to disclose.

EPO-169

Operative complications following microvascular decompression using autologous muscle graft to trigeminal neuralgia

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Background and aims: Trigeminal neuralgia (TN) is a painful and disabling syndrome which can be treated with microvascular decompression (MVD), a surgical blockage of the neurovascular compression.

Methods: This is a retrospective and descriptive study. The aim is to describe the operative complications of a case series of 40 patients diagnosed with TN and submitted to MVD with autologous temporal muscle graft between 2007 and 2020 in Sobral-Ceará, Brazil. Also, to present a discussion and literature review on the subject.

Results: Among TN patients, there was a predominance of women, with onset in the 6th decade of life, superior cerebellar artery (SCA) as the most affected vessel (75.0%), followed by the anterior inferior cerebellar artery (AICA) (17.5%). There was a success rate (total pain relief) of 92.5% (37 patients). A 57-year-old man of whom the target vessels were the SCA, AICA, and superior petrosal vein presented partial pain relief and hemiparesis. A 52-year-old woman presented partial pain relief, without post-operative complications. Death occurred intraoperatively in a 50-year-old woman of whom the target vessel was the transverse pontine vein.

Conclusion: MVD using autologous muscle graft is an efficient treatment for TN, though poorly discussed (to date, only six studies in the literature), especially regarding its complications. The observed complications of hemiparesis and death are unprecedented in the literature. The main postoperative complications reported are CSF leakage (50% of the studies), followed by fibrotic adhesions and transient facial palsy. Although uncommon, it is important to be aware of the possible complications of this technique.

Disclosure: The authors report no conflict of interest.

EPO-170

Treatment Satisfaction for Gene Silencing Pharmacotherapies in Hereditary Transthyretin Amyloidosis with Polyneuropathy

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[1] Akcea Therapeutics, Boston, United States, [2] QualityMetric Incorporated, LLC, Johnston, United States

Background and aims: Hereditary transthyretin amyloidosis (ATTRv) is a rare, progressive, systemic, fatal condition in which misfolded transthyretin proteins form amyloid in tissues and organs, often manifesting in polyneuropathy (ATTRv-PN). The FDA has approved two gene-silencing pharmacotherapies for ATTRv-PN: inotersen, administered subcutaneously; and patisiran, administered intravenously. Patient satisfaction for each treatment was examined during a period overlapping with the COVID-19 pandemic.

Methods: Patients with ATTRv-PN (with and without accompanying cardiomyopathy) in the United States participated in an observational, online survey between January 1st and October 25th 2020. The Treatment Satisfaction Questionnaire for Medication, version II (TSQMvII) was administered to 29 patients currently treated with inotersen (n=11) or patisiran (n=19). TSQMvII produces four scale scores – Effectiveness, Side Effects, Convenience, and Global Satisfaction – ranging from 0 to 100. Higher scores indicate greater satisfaction. TSQMvII scores were descriptively compared between treatment groups.

Results: Patients receiving inotersen indicated greater satisfaction with convenience than patients receiving patisiran (means 76.3 [standard deviation=19.4] vs. 58.6 [15.3], respectively), and less dissatisfaction with treatment side effects (86.1 [16.4] vs. 68.3 [19.0]). Ratings were comparable between treatments with respect to effectiveness (72.0 [21.5] vs. 67.1 [19.7]) and global satisfaction (78.0 [20.0] vs. 74.5 [21.7]).

Conclusion: While inotersen and patisiran were rated similarly in effectiveness and overall treatment satisfaction, inotersen was associated with less dissatisfaction of side effects, and greater convenience, with the latter possibly reflecting differences in mode of administration (i.e., at home vs. visit to a clinical site), which may be particularly important during a pandemic.

Disclosure: Funded by Akcea Therapeutics.

EPO-171

Patient-Reported Outcomes by Time from Symptom Onset to First Pharmacotherapy among Transthyretin Amyloidosis Patients

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[1] Akcea Therapeutics, Boston, United States, [2] QualityMetric Incorporated, LLC, Johnston, United States

Background and aims: Transthyretin amyloidosis (ATTR) is a rare, progressive, systemic, and potentially fatal condition in which misfolded transthyretin proteins form amyloid deposits in muscle and organ tissue. Currently available ATTR-related pharmacotherapies slow or stop the progression of amyloid deposition, but do not remove existing deposits. Because tissue and organ damage cannot be reversed, early treatment may be essential. These analyses examine the relations between time-to-treatment following symptom onset and long-term patient-reported outcomes (PROs) in patients with ATTR.

Methods: Several PROs, including the Composite Autonomic Symptom Scale, Norfolk Quality of Life-Diabetic Neuropathy questionnaire, and SF-36v2 Health Survey, were administered to 34 patients with ATTR (26 with nervous involvement) at initial and 12-month assessments in a longitudinal, observational, online survey study. Time-to-treatment was calculated as years between self-reported symptom onset and initiation of ATTR-related pharmacotherapy. Associations between time-to-treatment PROs at 12-months were examined using correlations, effect sizes for mean differences at yearly cut-points, and linear regression.

Results: Shorter time-to-treatment was at least moderately correlated with lower orthostatic hypotension (r=0.43); less vasomotor dysfunction (0.59), autonomic dysfunction (0.44), and large fiber neuropathy (0.51); fewer role limitations (0.48); and better health perception (0.46). Among the 24 PRO scores examined, effect sizes were at least moderate (i.e., d>0.5) for 17 scores at the 5-year time-to-treatment cut-point. Results from regression models were consistent. Similar patterns were observed for patients with only nervous system involvement.

Conclusion: Preliminary evidence supports early initiation of pharmacotherapy for patients with ATTR amyloidosis as vital for preserving health and quality of life.

Disclosure: Funded by Akcea Therapeutics.

Spinal cord and root disorders; Neurotoxicology/occupational neurology; Autonomic nervous system

EPO-172

Evaluation of cardiovascular autonomic function in hereditary transthyretin amyloidosis

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Background and aims: Autonomic dysfunction is a key feature of hereditary transthyretin amyloidosis (hATTR). In addition to causing prominent and disabling heterogenic manifestation (orthostatic hypotension, sweating disturbances, erectile and voiding dysfunction, etc.), it is believed that hATTR carries important prognostic value. The objective of this study was to assess in detail cardiovascular autonomic function throughout a battery of standardized autonomic tests in patients with genetically proven hATTR and healthy controls (HC).
Methods: Systolic and diastolic blood pressure (SBP, DBP), heart rate (HR) and breathing were continuously monitored at supine rest and during head-up tilt test (HUTT), Valsalva manoeuvre (VM), deep breathing (DB), cold face (IE) test and isometric handgrip (HG) in 10 hATTR and 16 HC.
Results: During HUTT, hATTR presented significantly lower SBP and DBP values compared to HC, and four hATTR patients fulfilled the criteria for orthostatic hypotension. Overshoot and Valsalva ratio were significantly lower in hATTR and pathological in all symptomatic patients. During DB, hATTR presented significantly lower respiratory sinus arrhythmia compared to HC and all symptomatic patients displayed pathological results. SBP, DBP and HR responses to HG were significantly reduced in hATTR compared to HC.
Conclusion: Both cardiovagal and cardiovascular adrenergic function are affected in hATTR; however, cardiovagal dysfunction was more diffused and pronounced.
Disclosure: Dr P Guaraldi has been advisory board member of Alnylam and received speaker fees and honoraria from Theravance Biopharma and Akcea Therapeutics.

EPO-173

Neurotoxicity related to the use of retinoids

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Background and aims: Retinoids are compounds chemically related to vitamin A, which are frequently used in dermatological practice. They are characterized by numerous mechanisms of action leading to normalization of keratinocyte proliferation and maturation. However, improper use of retinoids can induce neurologic complications.
Methods: We report the cases of three patients suffering from acne who received high doses of retinoids that lead to neurological complications.
Results: We report the cases of 30 and 27-year-old women who presented with severe acne treated immediately with high dose of oral Isotretinoin. They developed, two months after, severe headaches, vomiting and blurry vision. Brain MRI did not show an intracranial expansive process. The diagnosis of intracranial hypertension was established by measuring raised cerebrospinal fluid pressure. Etiological investigations were negative. Isotretinoin was stopped, with favorable clinical outcome. The third case was a 25-year-old woman with no medical history who presented a generalized tonic-clonic seizure 15 days after beginning treatment with high dose of Isotretinoin. Neurologic examination was normal. The brain magnetic resonance imaging and the electroencephalogram showed no abnormalities. Isotretinoin therapy was stopped with no recurrence of seizures.
Conclusion: Retinoic acid may produce neurotoxic symptoms of hypervitaminosis A. In this context, physicians should use caution in prescribing oral retinoid, and increase doses progressively. Large differences in individual susceptibility to vitamin neurotoxicity probably exist.
Disclosure: No disclosures.

EPO-174

Static compression of hand and foot perfusion for prevention of chemotherapy-induced peripheral neuropathy (CIN)

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Background and aims: CIN is common. Previous studies suggest protective effect of hand-compression with surgical gloves, presumably through reduced microvascular flow. This contradicts well-known autoregulatory effects. We tested the effect of static pressure-adjusted compression augmenting tissue oxygenation index (TOI) of hand and foot underlying neuroprotection.
Methods: 10 healthy young participants (50% male; age 24±4.7) wore two small-sized surgical gloves for 90 minutes. In the second experiment, consecutively, a compression sock and a calf stocking, all with a plantar insert and toe part (20–40 mmHg) were worn on one side for 30 minutes each. TO of the palm was continuously recorded at baseline, during compression at 5, 15, 30, 60 and 90 min and afterwards with near-infrared spectroscopy (NIRS) as well as hands and fingertips temperature with thermography of hand (TH) and foot (TF).
Results: In the hand compared to baseline, TOI (1.9±8.6, 4.1±0.3, 7.0±8.8, 8.4±8.1, 6.6±7.5%; p<0.001) and oxyhemoglobin (p=0.03) significantly increased time-dependently, total hemoglobin (THb) remained stable. TH was similar to other groups, TF remained stable. In foot calf stocking increased TOI (4.8±5.8, 6.8±6.4, 3.3±6.4%; p=0.042). Hydrostatic effects in the leg abolished all reactions post compression.

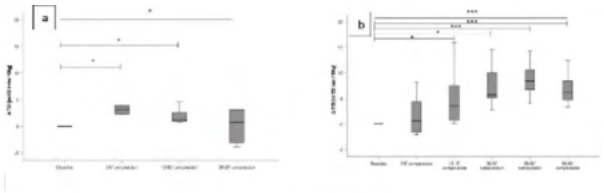

Figure 1: TOI_{AUC} changes during the treatment with surgical gloves (a) and with calf compression (b). Time-points of measurements: baseline (2 min pre-compression), during compression at: 5, 15, 30, (60, 90 min). *p≤0,05; **p≤0,01; ***p≤0,001.

TOIAUC changes during the treatment with surgical gloves and with calf compression.

Conclusion: In conclusion, first-time to our knowledge, we show that compression by surgical gloves increased TO in hands – and similarly in feet –, tilting the balance between microcirculatory oxygen supply and consumption with improved tissue oxygenation, providing a novel underlying mechanism, possibly involved in neuroprotection of CIN. This will have implications for the urgently needed therapeutic development of CIN-treatment of upper and lower extremities.
Disclosure: There are no financial conflicts of interest to disclose.

EPO-175

Effect of compression on local perfusion in development of a prevention of chemotherapy-induced peripheral neuropathy

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Background and aims: Chemotherapy-induced peripheral neuropathy (CIN) is common with limited treatment options. Previous studies suggest a protective effect of local hand-compression with surgical gloves, the postulated mechanisms being reduction of microvascular flow. Since this contradicts well-known autoregulatory effects, we tested the hypothesis that static pressure-adjusted compression has neuroprotective effects through improved tissue oxygenation (TO).
Methods: 12 healthy volunteers (50% male, age 22±1.6 years) wore a fabric compression glove on one side including a customized palmar insert to locally increase pressure (CCL II, pressure range 11–36 mmHg) for 5, 60 and 90min, respectively. In a second experiment, hands were cooled single-sided with ice-water. TO of the palm was continuously recorded bilaterally at baseline, during and after compression with near-infrared spectroscopy (NIRS) as well as hands and fingertips temperature with thermography.
Results: Temperature in compressed hand was significantly lower by 2.7° C at fingertips, compared with control hand after 90 min of compression (p<0.05 Wilcoxon). Compared to baseline, median Tissue Oxygenation Index (TOI, 5.5±5.1, 6.1±9.0, 11.2±7.0%, p<0.005 Friedman)) and oxyhemoglobin (O2Hb, 1.9±4.1, 5.7±5.8, 10.2±6.5µM/s, p<0.001 Friedman) significantly increased time-dependently, total hemoglobin (THb) remained stable. This contrasted with non-significant TOI and O2Hb changes after cooling of hands.

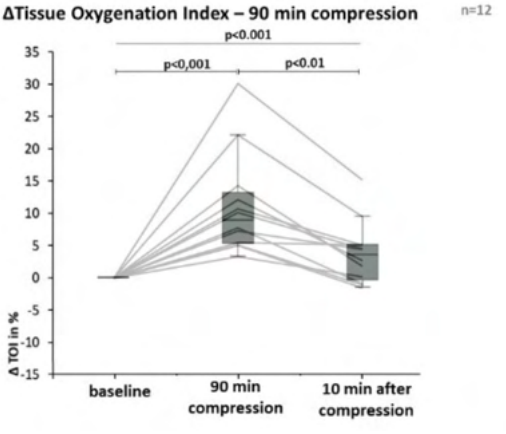

Fig. 1: Near infrared spectroscopic measurement of the hand before, during and after 90 min of local pressure-adjusted compression of 12 young, healthy subjects: changes in oxygenated hemoglobin (O2Hb)

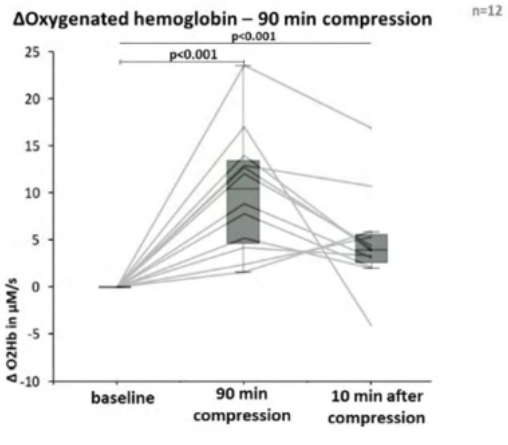

Fig. 2: Near infrared spectroscopic measurement of the hand before, during and after 90 min of local pressure-adjusted compression of 12 young, healthy subjects: changes in Tissue Oxygenation Index (TOI)

Conclusion: In conclusion, for the first time, to our knowledge, we show static pressure-adjusted compression of the hands tilting the balance between microcirculatory oxygen supply and consumption with improved tissue oxygenation, providing a novel underlying mechanism, possibly involved in neuroprotection of CIN. This will have implications for the urgently needed therapeutic development of CIN-treatment.
Disclosure: There are no financial conflicts of interest to disclose.

EPO-176

Acute Carbon monoxide poisoning, possibly a new etiology for CHANTER syndrome

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Background and aims: CHANTER syndrome (Cerebellar Hippocampal and Basal Nuclei Transient Edema with Restricted diffusion) is a novel clinicoradiographic syndrome that has been described mostly in adults with opioid neurotoxicity. Similarly, the acute brain lesions seen in carbon monoxide (CO) poisoning are also typically found in the basal ganglia (globus pallidus) and other areas vulnerable to hypoxia such as the hippocampus and the cerebral and cerebellar cortices, occasionally mimicking a drug intoxication.
Methods: We report the case of a 27-year-old woman with no particular medical history that was admitted in the Neurological Emergency Department with acute onset ataxia, severe dysarthria, confusion and headache. Her blood work showed increased white cells count and high levels of carboxyhemoglobin. Brain CT-scan and CSF analysis were normal. Brain MRI studies showed bilateral and symmetric restricted diffusion in the cerebellar cortex and hippocampus similar to that observed in CHANTER syndrome, but her toxicology screen was normal.
Results: A diagnosis of acute CO poisoning with neurological involvement was made and oxygen and anti-edema therapy was immediately started. Follow-up MRI showed important reduction of the cytotoxic edema accompanied by sustained clinical improvement
Conclusion: Our case illustrates a distinct radiological pattern of brain lesions produced by acute CO poisoning, therefore we propose it as a possibly new etiology for CHANTER syndrome.
Disclosure: Nothing to disclose.

EPO-177

Polyneuropathy as a Result of Occupational Mercury Poisoning in Different Parts of Industrial City

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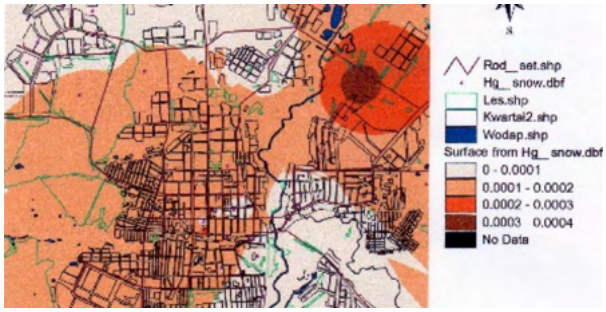
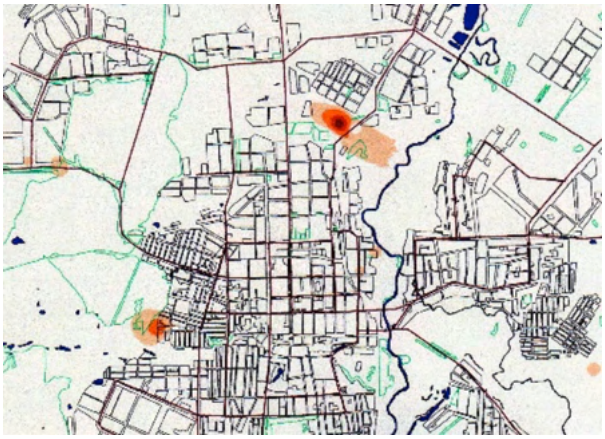
Background and aims: Chronic mercury poisoning (merculism) usually begins with mild symptoms of acute poisoning. In the future, general malaise, decreased appetite, and weight loss gradually develop. The affected person becomes nervous, weak and drowsy. The "mercury tremor" of the fingers, eyelids, lips and feet develops – typical signs of mercury neurasthenia and toxic neuropathy. Sensorimotor Polyneuropathy (SP) is an often result from inorganic mercury poisoning. Light Technology Plant (LTP) workers usually have inorganic mercury vapor exposure were noted to have prolonged motor and sensory ulnar distal latencies with abnormal needle EMG findings.



Mercury in Soil

Methods: We studied geographical distribution of two LTP in middle size industrial Russian city and level of the main immunity parameters in 164 these plants workers using IgA, IgM, and IgG detection by gel immunoprecipitation and CD4, CD4 and CD8 counting using immunofluorescence. We studied correlation between acuity of these patient neuropathy and their neurological and immunological involvement distribution of these patients in different areas of the city in connection to these plants location.
Results: It was found that those workers who worked longer years on these plans the symptoms of neuropaty were more severe. Most severe and chronic cases lived close by these LTPs. All these finding correlated with more deep involvement of immune system parameters in pathophysiology of these conditions and EMG findings in workers of LTPs.



Mercury in Trees

Conclusion: Combined methods of clinical and immunological evaluation with study of geography distribution of mercury pollution help to evaluate course and prognosis of toxic mercury SP as an occupational pollution condition.
Disclosure: Nothing to disclose.

EPO-178

Two cases of spontaneous spinal cord ischemic myelopathy

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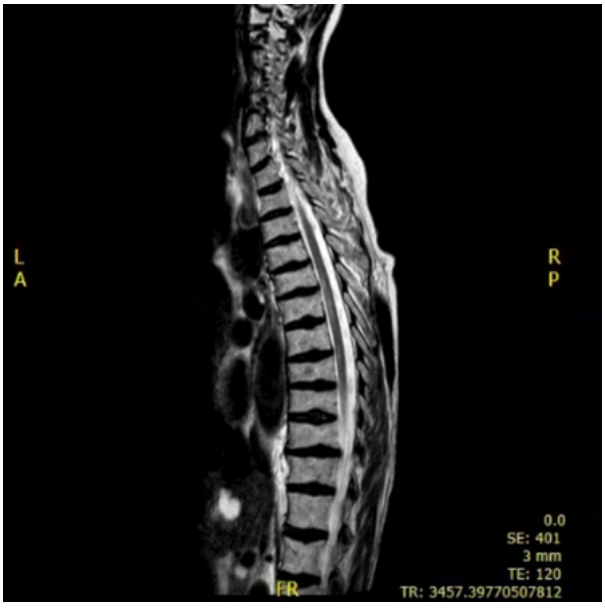
Background and aims: Spinal cord ischaemia accounts for less than 1% to 1.2% of all strokes. Spontaneous cord infarct and infarct following cardiac arrest are also rare.
Methods: Two cases of spontaneous spinal cord infarcts will be discussed. Clinical assessments with imaging and neurophysiological studies were done on those two patients.
Results: The first case was a 49 year old lady visiting the hospital collapsed in the hallway and she had a cardiac arrest. Down time was 30 minutes. She was successfully resuscitated. She recovered from the event without any cognition impairment. She had flaccid paraparesis with intact sensation to joint position, vibration and light touch with impairment of pin prick and cold/hot sensation to the level of T9/10. MRI brain and spines were normal. EMG/NCS revealed normal sensory nerves responses with motor CMAP abnormalities of tibial and peroneal nerves. The second case was 62-year-old lady with a sudden onset both legs weakness. This progress in a few hours and weakness became complete in 10 hours. There was no sensory symptom. She developed constipation and urinary incontinence, and bilateral gluteal area pain later. She has complete paralysis of both legs with areflexia. Sensory exam finding was exactly like the first[t] patient at T7/8 level. Brain MRI brain was normal. MRI of spinal cord showed changes (attached findings/images). Thoraco-abdominal aorta imaging and EMG/NCS were unremarkable.



MRI of case number 2

Conclusion: Neurological evaluation remains the key in reaching a diagnosis of spinal cord ischemic myelopathy. The value of imaging in ischemic conditions for spinal cord is significantly less than that of brain.
Disclosure: Nothing to disclose.

EPO-179

Atypical presentation of a spinal arteriovenous fistula with clinical-radiological dissociation

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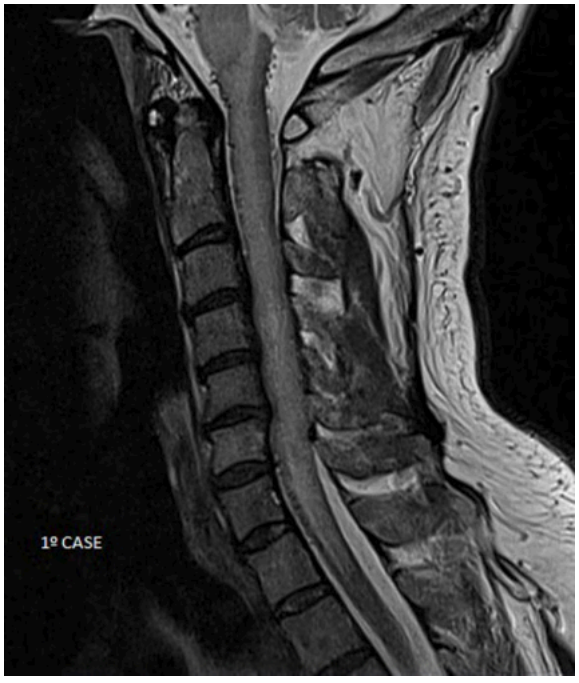
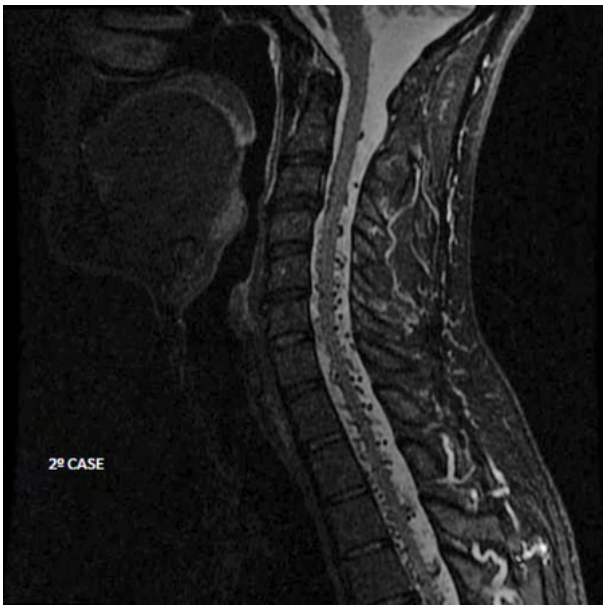
[1] Neurología, Guadalajara, Spain, [2] Guadalajara, Spain, [3] Madrid, Spain

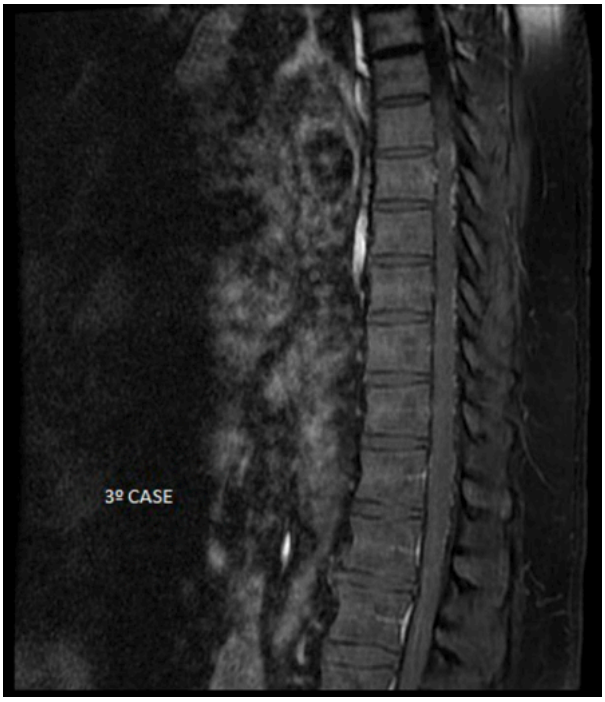
Background and aims: The diagnosis of Spinal arteriovenous fistulas (SAVFs) constitutes a challenge given the great variability of clinical presentation, being a pathology always to be taken into account since they associate great morbidity without early treatment.
Methods: Our objective is to expose through three clinical cases the variability of clinical presentation of SAVFs and the clinical-radiological dissociation.
Results: 1st Case: 54-year-old male complains of progressive cervical pain resistant to treatment for 40 days. The physical examination (PE) highlights paresthesia in both hands, claudication of the right lower limb without touching the bed line, maintaining a slightly paretic gait. Exalted reflexes in both lower limbs. 2nd Case: 48-year-old male who reports paresthesia of the 2nd–4th left toe of one year of evolution without other associated symptoms. PE: hypoesthesia in the plantar aspect of the 2nd–4th toe of the left foot without alterations at the motor level or in reflexes. 3rd Case: 42-year-old male who presents episodes of acute urine retention. Months later, weakness appears in the lower limbs at the proximal level. PE: Bilateral increase in tone in the lower limbs that conditions spastic gait with hypoesthesia in the buttocks.



1º case.



2º case.



3º case.

Conclusion: The diagnosis of SAVFs is extremely difficult due to the initial clinical variability; in our three cases the presentation has been atypical (neck pain, foot paresthesia, acute urine retention), which requires a high level of clinical suspicion. We highlight the clinical-radiological dissociation in all of our cases, the signs of greater myelopathy not corresponding in magnetic resonance with greater clinical involvement.
Disclosure: I have not received commercial or institutional support.

EPO-180

Multiple Extradural Spinal Arachnoid Cysts: A Case-based Update

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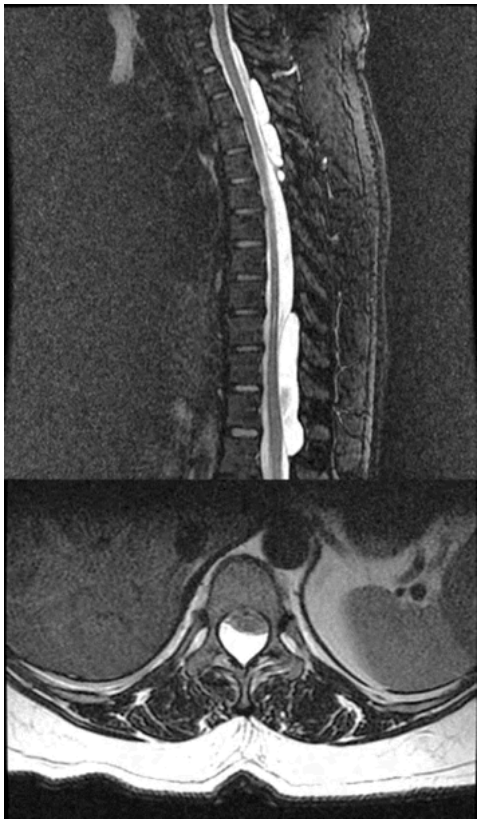
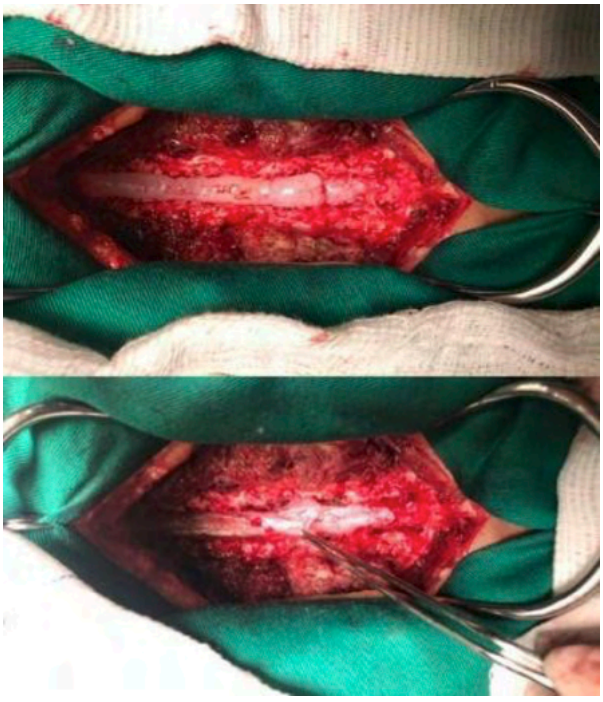
Background and aims: Arachnoid cysts are CSF diverticula. Extradural spinal arachnoid cysts (SACs) are rare spinal cord lesions that can cause nervous compression and disability.
Methods: Retrospective chart review of clinical data and magnetic resonance imaging (MRI) of a patient who presented with multiple extradural SACs. A discussion and literature review are presented, focusing on this unique manifestation of the condition, as well as its chosen treatment, targeting only the symptomatic lesion.
Results: A 38-year-old woman presented with back pain, hyperreflexia, and a history of t wo episodes of falling due to transient weakness in the lower limbs. MRI revealed multiple extradural spinal arachnoid cysts between the T3-L1 vertebrae. She underwent a complete surgical resection of the symptomatic arachnoid cyst with good postoperative recovery. Intraoperatively, a type I extradural SAC was confirmed.



Preoperative imaging. (a) Midsaggital T2WI with fat suppression MRI demonstrating multiple (4) extradural spinal arachnoid cysts at T3-T5 and T10-L1 levels. (b) Axial T2 MRI demonstrating the symptomatic cyst with spinal cord compression at the T11 level.



Intraoperative imaging. View of the point of communication with the CSF space through the dura laterally, at the T11 level (type I extradural spinal arachnoid cyst).

Conclusion: The occurrence of multiple extradural SACs is a rare disease manifestation, with only 31 cases reported in the literature, of which only seven were treated with a partial removal – resection of just the symptomatic lesions. This disease can be classified as primary or secondary – eg, associated with previous epidural haematoma -, although its pathogenesis remains unclear. The clinical manifestations can include pain, gait ataxia, paresthesia, urinary and/or intestinal incontinence, and paralysis. MRI is recommended for a location-based classification. Surgery is the main treatment. A partial surgical approach targeting only the symptomatic lesions appears to be a good therapeutic option. Although rare, it is important to be aware of and understand the possible presentation of multiple extradural SACs.
Disclosure: The authors report no conflict of interest.

EPO-181

Epidemiological profile of patients undergoing correction of myelomeningocele in Brazilian public health system

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Background and aims: Myelomeningocele is characterized by an externalization of the spinal cord, surrounded by epithelial tissue, affecting any vertebral segment and which represents an important impact on the morbidity of these patients. The epidemiological understanding of this abnormality is of great importance for public health, since based on these data, prevention strategies can be designed, as well as treatment and assistance for families. The objective of this work is to report an epidemiological profile of myelomeningocele in Brazil, analyzing its incidence among socioeconomic regions.
Methods: This is a descriptive observational, cross-sectional study, composed of secondary data published by the Ministry of Health through DATASUS and extracted from the Unified Health System (SUS) Hospital Information System (SIH/SUS). A period of 12 years was selected (January 2008 - December 2019) and general data on hospital morbidity, by place of hospitalization, covering the entire Brazilian territory
Results: A total of 12,079 patients were hospitalized for myelomeningocele in the studied period, the majority of which (5,527) in the Northeast and Southeast (3,889) of the country. This data corroborates the socioeconomic situation of the Northeast region and the consequent carelessness with exams and prenatal care, both in the number of consultations and in folate deficit supplementation, related to the malformation, in populations with precarious situations; differently from the region Southeast, whose high number reflects the absolute population of the region.
Conclusion: In Brazil, more investments in prenatal care, mainly in the Northeast region, and hospital care are needed for patients with myelomeningocele.
Disclosure: Nothing to disclose.

EPO-182

Decompression sickness or something else?

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Background and aims: Decompression sickness is a rare diving related injury that can result in severe and disabling neurological consequences.
Methods: N/A
Results: A 45-year-old male, a recreational diver with no known personal history of neurologic dysfunction presented to the emergency department with a vertiginous syndrome after a 6-hours scuba-diving ascent. He was diagnosed with possible decompression sickness and treated with hyperbaric oxygen. 48 hours later he developed hypoesthesia of the left lower limb. On examination, there was a sensory level at D9 on the left side, loss of pinprick sensation at the right hand and mild tandem gait ataxia. Brain MRI showed hyperintensities in T2-FLAIR images involving the corona radiata and subcortical white matter of the frontal lobes bilaterally. Thoracic spinal cord MRI revealed two areas with restricted diffusion on the posterior aspect of the cord at D7-D8 and D9-D10. The possibility of multiple sclerosis was discussed, though blood and CSF analyses were unremarkable. Follow-up brain MRI at three months showed identical findings while the thoracic spinal cord MRI revealed a complete resolution of the previously described lesions. On revaluation, three months later the patient only presented with residual mild tandem gait ataxia.
Conclusion: This case highlights that although there may be similarities between the neurological presentation of decompression sickness and multiple sclerosis, the temporal relationship between scuba diving, the onset of symptoms, and imagiologic features suggests that decompression was the cause of these lesions, as corroborated by the CSF findings and complete resolution on MRI follow up.
Disclosure: Nothing to disclose.

EPO-183

Case Report of Esophageal Ulcer Due to Anterior Cervical Arthrodesis

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Background and aims: From degenerative diseases to traumas, the technique of anterior cervical arthrodesis has been widely used. Nevertheless, its intraoperative and post-operative complications should be considered, ranging from loosening of the screws to lesions of the upper digestive tract. This case report aims to discuss possible interventions in the face of a common injury resulting from anterior cervical arthrodesis.
Methods: The data collected for this study were obtained from medical records belonging to the Roberto Santos General Hospital, located in Salvador, Bahia.
Results: This is a 60-year-old-female and tetraplegic patient, who came to the emergency unit complaining of dysphagia for five years. She reports a motorcycle accident in 2002, being submitted to anterior cervical arthrodesis surgery on the C4 and C5 vertebrae, with tetraplegia as a sequel. In January 2020, due to dysphagia, she underwent upper digestive endoscopy, which showed an esophageal ulcer associated with a metallic component. For this patient, a conservative treatment was chosen, without surgical intervention for the lesion, associated with gastrotomy in order to interrupt esophageal food flow. Until the end of data collection, there was no return of the patient to the emergency department.
Conclusion: This case depicts a common complication of a cervical arthrodesis, an esophageal ulcer, however, without aggravating complications, such as infection. For this reason, therapies need to be discussed for the medium and long-term benefits. In this case, the conservative approach proved to be efficient, adopting as a criterion the absence of complications and return of this patient to the hospital.
Disclosure: Nothing to disclose.

EPO-184

Common concomitant causes of paraparesis, approach to relevance of clinic evaluation

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Background and aims: Vitamin B12 is essential for neurological function and its deficiency is associated with many neurological disorders such as peripheral neuropathy, ataxia, dementia, myeloneuropathy psychosis.
Methods: We report the case of a 59 year-old woman, who presented with a 6-month history of generalized body weakness, difficulty walking and lumbalgia. A lumbar MRI was performed and a L4-L5 hernia was detected.The patient was performed a hernia repair surgery, but after two weeks she became clinically worse with difficulty moving both legs. She also had hallucinations and episodes of short-term memory loss. The patient was conscious, but disoriented to place, time, and person. During the neurological examination, she was unable to support herself while standing. All cranial nerves were intact. The lower limbs had a power rating of 2/5 symmetrical. There was pain in the lower limbs on passive movement,burning sensations in both legs and a positive Babinski sign. The patient had a score of 16/30 on the Mini Mental State Examination. The rest of the examination was unremarkable.
Results: Metabolic workup showed severe vitamin B12 deficiency (83 pg/ml), decreased reticulocyte count, and increased direct bilirubin and lactate dehydrogenase. Intramuscular injection of cobalamin showed significant improvement.
Conclusion: In conclusion, we want to emphasize the importance of assessing the B12 levels in patients presenting with new onset of depressive disorders, paraparesis and gastrointestinal symptoms.If vitamin B12 deficiency remains undiagnosed, serious sequelae may occur. If vitamin B12 deficiency remains undiagnosed, serious sequelae may occur.
Disclosure: Nothing to disclose.

EPO-185

Clinical and MRI improvement in Hirayama Disease following conservative treatment

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Background and aims: Hirayama disease (HD) is a rare disease that predominantly affects males in their 20s. Classical findings are muscle atrophy and weakness of the forearms and hands, either bilateral or unilateral, without sensory changes. It is described as cervical myelopathy due to neck flexion. Magnetic resonance imaging (MRI) in cervical hyperflexion confirms the clinical diagnosis.
Methods: The patient presented with complaints of weakness in his left hand. He underwent physical and neurological examinations (NE); Nerve conduction studies (NCS), Electromyography (EMG), serum Creatine phosphokinase (CPK) and Cerebrospinal fluid (CSF) studies, Serum and CSF electrophoresis, Echocardiography and dynamic contrast MRI. Conservative treatment with cervical collar and physiotherapy was initiated.
Results: NE at 21 and 30 years of age revealed improvement in muscle weakness with non-progressive distal muscle hypotrophy of the left upper limb. Bilateral poly-mini-myoclonus of the fingers on extension was observed. Sensory deficits were absent and deep tendon reflexes were intact. NCS of the median and ulnar nerves showed reduced compound motor unit action potentials (MUAPs) with slightly reduced motor conduction velocity on the left side. Needle electromyography showed high-amplitude, long-duration MUAPs. After a 10-year follow-up, MRI studies showed reduction in the characteristic crescent shaped posterior epidural space in neck hyperflexion with decreased enhancement after gadolinium administration.
Conclusion: HD is rare among the European population and in cases of clinical suspicion, a dynamic contrast MRI should be conducted. Early diagnosis is critical for instituting conservative treatment with cervical collar and physiotherapy in order to halt the disease progression.
Disclosure: No disclosures.

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EPO-186

Stereological estimation of neuronal volume in the human entorhinal cortex

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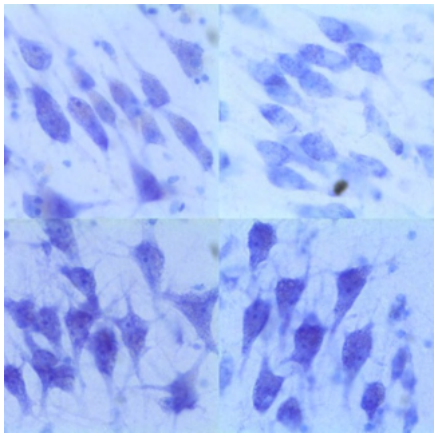
Neurology, Murica, Spain

Background and aims: This dissertation is focused on the stereological analysis of the volume of neuronal soma in the entorhinal cortex. This region is located in the ventromedial region of the temporal lobe and is integrated into a set of regions, anatomically and functionally related, that receive the denomination of formation of the hippocampus. The importance of the entorhinal cortex in learning, spatial navigation and memory formation and the alteration of these functions during physiological ageing justify the purpose of our study.
Methods: Our study consists of the analysis of the existence of changes in the volume of the neuronal soma associated with age. We have conducted a study of the entorhinal cortex in eight human brains (<65 years and >65 years, n=4 for each group), obtaining stereological information to establish contrasts between age groups. The study was extended in order to contrasts between groups by sex, gender, hemisphere, entorhinal cortex region (lateral or medial) and layer (II, III, V and VI).



Neurons of the entorhinal cortex layers II, III, V and VI

Results: The data obtained reflect a similar volume of the neuronal soma in all the groups analysed. The results show that the size is greater in women and in the right hemisphere, but without reaching statistical significance in any case.
Conclusion: Working with a small sample implies a low statistical significance of the results and, therefore, makes it impossible to extrapolate them to the general population. However, it could serve as a starting point for future investigations of the entorhinal cortex with a larger sample size.
Disclosure: Nothing to disclose.

EPO-187

Non-White Cases of Sporadic Creutzfeldt-Jakob Disease: A 28 year Review of United Kingdom National Surveillance Data

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Background and aims: Descriptions of sporadic Creutzfeldt-Jakob disease (sCJD) in non-White populations are limited. Improved understanding may aid diagnoses and case ascertainment within surveillance programmes. We aimed to: 1) Ascertain the proportion of cases with sCJD with non-White ethnicity in the United Kingdom (UK) and, 2) Compare clinical characteristics and investigation findings between non-White and White cases.

Methods: We analysed records of all cases of probable and definite sCJD assessed by the UK National CJD Research and Surveillance Unit over a 28 year period (1990–2017). Cases were stratified into White and non-White groups. Demographics, clinical features, investigation findings, and post-mortem numbers were compared.

Results: 1,697 sCJD cases were included: 1,642 (97%) White, 55 (3%) non-White (Asian/Asian British, Black/African/Caribbean). The number of non-White cases is 7% lower than the proportion this population make up in the UK ($p<0.001$). Age at symptom onset was four years lower in the non-White population ($p=0.007$). Clinical and investigation characteristics were otherwise similar between ethnic groupings. The autopsy rate in non-White cases and classification as definite sCJD were 30% and 24% lower ($p<0.001$) respectively in comparison to White cases.

Conclusion: Approximately 3% of all cases of sCJD in the UK are non-White, despite this group representing approximately 10% of the UK population. Non-White cases tend to be younger and likelihood of autopsy is lower; relevant considerations for surveillance programmes. Reasons for under-representation of sCJD cases in non-White populations are unclear and merit further evaluation.

Disclosure: Nothing to disclose.

EPO-188

Primary progressive aphasia and bio-imaging biomarkers: about three cases in Tunisia

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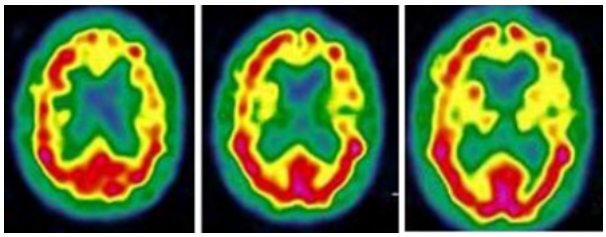
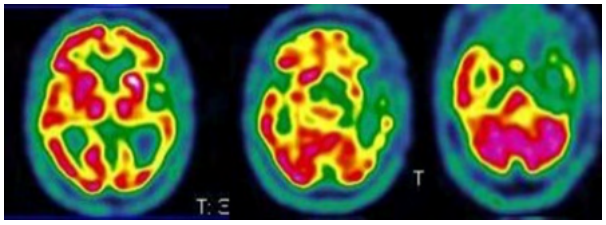
Background and aims: Primary progressive aphasias (PPA) are a group of focal dementias caused by degeneration of brain systems that govern language. The pathophysiology's complexity can be at the origin of PPA diagnosis difficulty. Therefore, confronting clinical data with neuro-imaging markers is of crucial interest.

Methods: We selected patients who consulted in our neurology department for degenerative dementia between January and June 2018. All subjects underwent a neurological examination and had cerebral magnetic resonance imaging, single-photon emission computed tomography and a lumbar puncture with dosage of CSF biomarkers: T-tau, P-tau and amyloid- peptide. We used Mesulam 2003 criteria to retain the diagnosis of PPA.

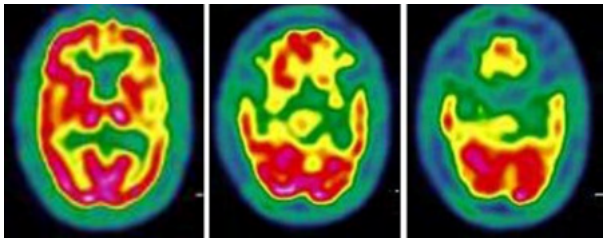
Results: We collected three patients (2 men and one woman) with a neuropsychological profile suggestive of PPA. The mean age was 62. The nature of language disorders varied according to the sub-type of the PPA. All patients had episodic memory impairment and patient n°1 had a frontal syndrome. Neuroimaging was normal for patient n°1, showed atrophy of temporal lobes for patient n°2 and of temporo-parietal region for patient n°3. Cortical hypoperfusion affecting the dominant hemisphere, which topography depended on PPA variants, was noted in all patients. CSF biomarkers profile was normal in patient n°1 presenting agrammatic PPA and n°3 presenting logopenic PPA and was suggestive of Alzheimer disease lesion in patient n°2 presenting semantic PPA with T-tau at 1,120 and P-tau at 93.



SPECT showing a typical scintigraphic aspect of a NFPPA with frank hypoperfusion of the left perisylvian region extended to the ipsilateral dorso-lateral prefrontal cortex in a right-handed patient



SPECT showing a typical aspect of SPPA with absence of left temporal pole infusion including left internal temporal structures in a right-handed patient.



SPECT showing a typical aspect of a LPPA with hypoperfusion of the left perisylvian region in a right-handed patient associated to hypoperfusion of both parietal cortexes, predominated at left, and of bilateral internal temporal structures.

Conclusion: Bio-imaging markers have an important role in making an accurate and early identification of PPA syndromes and can be helpful in clinical counselling and appropriate management.

Disclosure: The authors do not disclose any conflict of interest.

EPO-189

Adverse perinatal outcomes and risk of epilepsy after traumatic brain injury: A Danish nationwide cohort study

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Background and aims: Traumatic brain injury (TBI) and adverse perinatal outcomes, such as premature delivery, low birth weight and low Apgar score are risk factors for epilepsy. However, it is not well described how the interaction between adverse perinatal outcomes and TBI affects the risk of epilepsy after TBI. We studied whether the risk of epilepsy after a TBI was modified by adverse perinatal outcomes.

Methods: We performed a nationwide register-based cohort study of all singletons born in Denmark between 1 January 1982 and 31 December 2011 who were alive and residing in Denmark on their fifth birthday. Subjects were followed from this day until onset of epilepsy, death, emigration from Denmark or 31 December 2016, whichever came first. Cox regression models were used to estimate hazard ratios (HR) of epilepsy after TBI and interactions with gestational age at birth, birth weight, and Apgar score.

Results: We found an increased risk of epilepsy with lower gestational age at birth, birth weight, and Apgar score. The risk of epilepsy was also increased after a TBI (HR 2.40, 95% CI 2.26–2.54), but this association was not modified by either gestational age at birth (p=0.2579), birth weight (p=0.7354), or Apgar score (p=0.1501) (see Table 1).

	Persons without TBI		Persons with TBI		
	Persons with epilepsy (N=)	*Crude IR (per 1000 years)*	*Persons with epilepsy (N=)*	*Crude IR (per 1000 years)*	*HR (95% CI)**
Gestational age at birth					
<32 weeks	190	1.63	14	2.82	1.90 (1.11-3.28)
32-36 weeks	829	0.90	53	1.46	1.77 (1.34-3.28)
37-38 weeks	2581	0.76	215	1.70	2.53 (2.20-2.91)
39-41 weeks	11670	0.67	935	1.43	2.43 (2.27-2.60)
>41 weeks	1464	0.69	120	1.46	2.36 (1.96-2.85)
Birth weight					
<2000 g	387	1.38	28	2.32	1.93 (1.31-2.83)
2000-2499 g	553	0.92	53	2.06	2.42 (1.83-3.21)
2500-2999 g	2282	0.81	195	1.68	2.37 (2.04-2.74)
3000-3999 g	10778	0.67	864	1.43	2.45 (2.28-2.63)
>3999 g	2734	0.66	197	1.37	2.29 (1.98-2.65)
Apgar score					
<7	240	1.50	11	1.71	1.10 (0.60-2.01)
7-8	468	0.92	37	1.90	2.30 (1.65-3.22)
9	739	0.82	63	1.86	2.56 (1.98-3.31)
10	15287	0.68	1226	1.46	2.42 (2.28-2.57)

* Each model was adjusted for age, sex, calendar year, residual measures of adverse perinatal outcomes, cerebral palsy, congenital malformations of the nervous system, maternal age at birth, maternal educational level at birth, maternal civic status at birth, parental epilepsy, and pre-eclampsia and hypertension during pregnancy.
IR = Incidence rate; HR = Hazard ratio; CI = Confidence interval

Table 1: Hazard ratios of epilepsy by traumatic brain injury and adverse perinatal outcomes

Conclusion: Adverse perinatal factors did not modify the risk of epilepsy after TBI.

Disclosure: This study was supported by the Novo Nordisk Foundation (NNF16OC0019126 and NNF17OC0029860), the Central Denmark Region, and the Danish Epilepsy Association.

EPO-190

Lack of sex differences in the cognitive function in healthy elderly

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Background and aims: Epidemiological studies have shown a sex difference in the cognitive dysfunction in the elderly where women are more susceptible to Alzheimer's disease. Evidence has reported that physical activity (PA) is an important strategy for brain health, but the exact mechanism by which PA would promote beneficial effects is not fully understood. This study aimed to examine the sex differences in the cognitive function in the elderly according to the level of PA.

Methods: This study was approved by the Ethical Committee Board from Medical School/UNIMES (Number: CAAE 20938619.4.0000.5509). 98 participants were eligible for the study. Inclusion criteria were >65 years-old, non-smoking, no severe cognitive impairment, preserved activities of the daily living. Cognitive function was assessed by the mini-mental state examination (MMSE) and the level of PA was evaluated by Baecke questionnaire for older.

Results: The participants were divided into physically inactive (G1, Baecke score 9, for men and women). Overall, the number of participants in the G1 (n=71) was greater than G2 (n=27). We did not find sex differences in all parameters between the two groups.

Conclusion: The cognitive function is well preserved in the healthy elderly that was independent of the sex and the level of PA.

Disclosure: Financial Support: São Paulo Research Foundation (FAPESP)

EPO-191

Autonomic dysfunction in Frontotemporal Lobar Degeneration: clinical and MRI analysis

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Background and aims: In Frontotemporal Lobar Degeneration (FTLD), sparse studies have reported autonomic symptoms in behavioral-variant FTLD (bvFTD) and semantic dementia (SD), and particularly, in association with c9orf72 mutations. Also, an association between focal temporal lobe atrophy (FTLA) and pain and temperature symptoms has been described. Our aim was to identify autonomic symptoms in FTLD patients and to assess any relation with brain atrophy profile.

Methods: We retrospectively reviewed clinical data on 190 patients diagnosed with FTLD between 2007–2019 at the Memory Clinic of our Neurology department. Nineteen patients (10%) with autonomic symptoms were identified, and when available, each patient's brain MRI was reviewed.

Results: Mean age (years) was significantly different between patients with (70.98.0) and without (63.88.9) dysautonomia (p=0.01). Eight patients (41.1%) had early urinary incontinence, four (21%) thermoregulation dysfunction, four (21%) early erectile dysfunction, three (15.8%) chronic diarrhea, one (5.3%) orthostatic hypotension, and one (5.3%) hypersomnia. Considering clinical variants, autonomic symptoms were present in 15/166 (9%) bvFTD patients, 2/16 (12.5%) progressive non-fluent aphasias (PNFA), 2/8 (25%) SD and 2/7 (28.6%) right-temporal-variants (rtvFTD). 10 in 156 sporadic forms (6.4%) had autonomic manifestations while 9/34 genetic forms (27%) had dysautonomia, namely, 6/13 patients with c9orf72 mutation (46.1%) and 3/21 progranulinopathies (14.3%). Thermoregulation dysfunction was preferentially associated with rtvFTD and c9orf72 mutation. Visual review of MRI scans of patients with dysautonomia (n=11) revealed an over-representation of cases with relatively FTLA (2 right-sided, three left-sided).

Conclusion: Autonomic symptoms were more prevalent in temporal-variants and genetic forms, particularly c9orf72 carriers. Thermoregulation dysfunction was linked to rtvFTD and c9orf72 mutations.

Disclosure: The authors report no disclosures.

EPO-192

Comparative study of cerebral blood flow patterns by perfusion MRI between dementia patients and healthy population

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Background and aims: Dementia is a common and disabling process with numerous psychological and social consequences for patients. In this study structural and Arterial spin labelling perfusion MRI was performed to evaluate demented patients.

Methods: In this survey, 51 individuals in four groups were enrolled as follows: 15 Alzheimer patients, nine patients with vascular dementia, 10 subjects with MCI and 17 individuals with normal cognition. After collecting demographic information, past medical history and performing mini mental state exam, MRI was done in all patients. Finally, data related to brain structural and perfusion changes (after ASL data quantification and cerebral blood flow (CBF) extraction) were assessed and analyzed in SPSS.

Results: In visual rating scales maximum global cortical atrophy (GCA) was seen in the Alzheimer group, with CBF decreasing by GCA score increase. Also by increasing in medial temporal lobe atrophy (MTA score) and parietal lobe atrophy (Koedam score) cerebral blood flow reduction was shown in temporal and parietal lobes respectively. Hypoperfusion in bilateral temporal and parietal lobes was declared in Alzheimer and MCI in comparison with normal cognition and in Alzheimer in comparison with MCI. Maximum amounts of white matter hyperintensities (WMH) were found in vascular dementia and with WMH volume addition and FAZEKAS score increasing, cerebral blood flow reduction was noted.

Conclusion: Brain atrophic changes are in accordance with cerebral perfusion in Alzheimer´s disease. There is reverse relationship between age and cerebral blood flow in MCI and Alzheimer patients and direct relationship between cerebral blood flow, MMSE score and cognition state.

Disclosure: Nothing to disclose.

EPO-193

Rapid cognitive decline associated with anti-glutamic acid decarboxylase autoantibodies (GAD): a case report

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Background and aims: Antibodies to glutamic acid decarboxylase (GAD) have been associated with several neurological syndromes, including stiff-person syndrome (SPS), cerebellar ataxia and epilepsy. However, the full spectrum of symptoms related to anti-GAD is still unclear and not well defined, since it has been linked to other conditions, such as cognitive decline.

Methods: We describe the clinical course of a patient with cerebellar ataxia due to anti-GAD who, after years of clinical stability, developed SPS and a rapid cognitive decline.

Results: A 50-year-old woman with progressive cerebellar ataxia underwent an extensive study, finding anti-GAD antibodies positive in serum (tested by radioimmunoassay; titer 23,000 U/mL; and subsequently confirmed by Immunoblot). By the age of 61, she progressively started with muscle cramps and rigidity, symptoms that were consistent with SPS and episodes of confusion and disorientation. Within one year and a half, she developed a rapid cognitive impairment (from 19/30 in the Minimental State Examination (MMSE) test to 9/30). Repeated MRIs showed significant vermal atrophy without other alterations. A brain SPECT was performed, consistent with frontotemporal dementia. Blood tests excluded other causes of dementia. Several courses of intravenous immunoglobulin (IVIg) were administered, following SPS improvement, but with no benefit in the cognitive decline.

Conclusion: Very few publications analyse the presence of cognitive impairment related to anti-GAD antibodies, although an association seems to exist. Due to a low index of suspicion and its lower frequency compared to other more florid syndromes, dementia associated with these autoantibodies could go unnoticed and not be optimally treated.

Disclosure: Nothing to disclose.

EPO-194

Association of CAG repeat length in HTT gene with CSF tau in subjective cognitive decline and mild cognitive impairment

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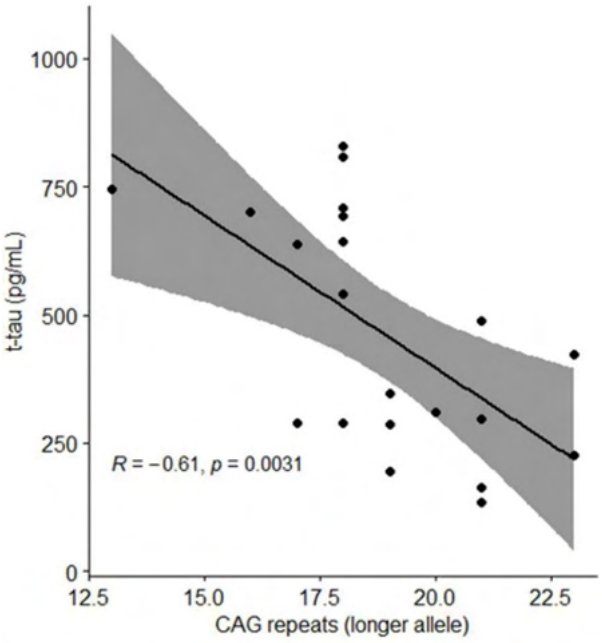
Background and aims: HTT is a gene containing a key region of CAG repeats. When expanded beyond 39 repeats, Huntington disease (HD) develops. Individuals with less than 35 repeats are not associated with HD. Wild-type HTT protein has been showed to be neuroprotective and a higher number of repeats in HTT, below disease threshold, has been linked to advantageous changes in brain structure. We aimed to evaluate the effect of CAG repeat length on CSF biomarkers of Alzheimer's disease in patients with subjective cognitive decline (SCD) and mild cognitive impairment (MCI)
Methods: We included 21 patients (11 SCD and 10 MCI). All patients underwent an extensive neuropsychological battery, analysis of HTT alleles and CSF analysis for measurement of A1-42, A1-42/40, t-tau and p-tau.
Results: CAG repeat number in the shorter HTT allele was inversely correlated with t-tau concentration (=-0.61, p=0.031). This relationship still remained when adjusted for confounding factors, including A status. When we grouped patients according to t-tau positivity (>400pg/mL, 11 T+ and 10 T-), we found that the inverse correlation between CAG repeat length and tau concentration was confirmed only in T+ patients (=-0.68, p=0.023). Moreover T- patients had more CAG repeats compared to T+ patients (19.50±2.25 vs. 18.00±1.00, p=0.043).
Conclusion: In patients with positive t-tau concentration indicating neurodegeneration, higher CAG repeat length in the shortest HTT allele is associated with lower concentration of t-tau CSF. Further studies are needed to explore if this association is due HTT neuroprotective effect.



Correlation between CAG repeat lengt and CSF t-tau concentration in the whole sample

Disclosure: The authors declare that they have no conflict of interest.

EPO-195

New biomarker of neurodegenerative disease

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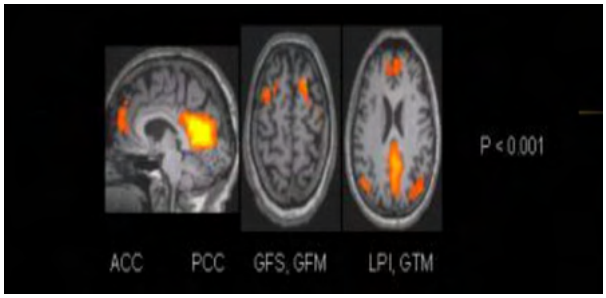
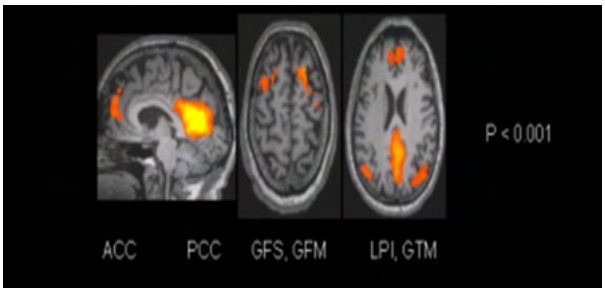
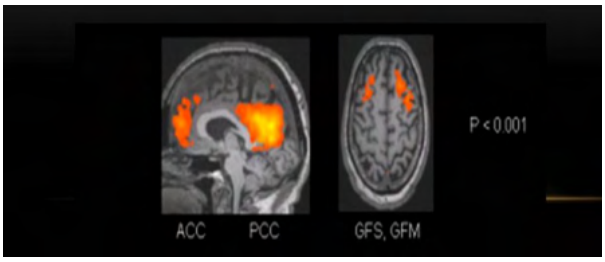
Background and aims: Alzheimer's disease (AD) selectively involvoves cerebral neuronal networks.The aim was to correlate fMRI patterns and EEG-coherence in Alzheimer's disease (AD), amnestic Mild cognitive impairment (aMCI), non amnestic Mild cognitive impairment (nMCI) and controls.
Methods: 65 patients with AD, 60 aMCI, 57 nMCI and 60 age-matched controls underwent fMRI (3 Tesla ,TRIO, Siemens) and resting EEG-recordings (NeuroScan Synamps System). EEGs were recorded using a standard protocol and montage. Coherences between regions of interest, based on fMRI activation patterns were calculated.
Results: There were significant differences between AD and aMCI for theta coherences between anterior cingulate gyrus (ACC) and left temporal gyrus (LTG) (AD<aMCI, p<0,05); between AD and controls for theta between ACC and right temporal gyrus, between ACC and left hippocampus, and between ACC and right parietal gyrus (AD<controls, p<0,01). aMCI-subjects showed reduced coherence compared with controls between ACC and left frontal superior gyrus within delta, theta and alpha1-band. Theta coherence was significantly between anterior and posterior cingulate gyrus, between right and LTG (aMCI< controls, p<0.05). There were significat differences between nMCI and controls between ACC in delta and theta (nMCI <controls, p<0.05).There were not found significant differences between AD and nMCI.



Comparison of healthy elderly subjects vs. aMCI patients. fMRI activations (p<0.001). Correspondence in frontal, but not in posterior regions.



Comparison of healthy elderly subjects vs. AD patients. fMRI activations (p<0.001) . Correspondence in frontal, but not in posterior regions



Comparison of aMCI and AD patients. fMRI activations (p<0.001) . Correspondence in posterior regions

Conclusion: EEG coherence seems to be a useful approach, which helps to detect the early stage of cognitive decline.
Disclosure: Nothing to disclose.

EPO-196

Functional connectivity as predictor of transformation from amnestic mild cognitive impairment to Alzheimer's disease.

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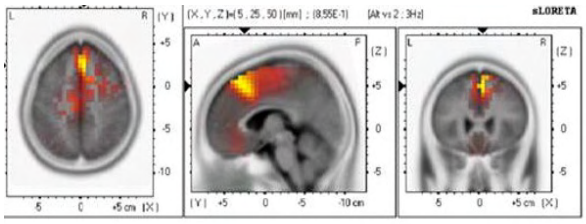
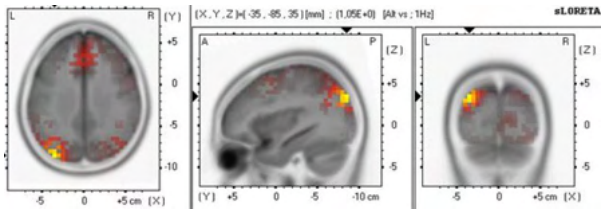
Background and aims: Alzheimer's disease (AD) is a neurodegenerative disorder. Amnestic mild cognitive impairment (aMCI) is predementia condition. EEG-coherence is sensitive marker of functional connectivity, whereas fMRI detect activation patterns, which could be coupled. The aim was to correlate fMRI activation patterns and EEG-coherence in AD,aMCI and age-matched controls.
Methods: 67 AD patients, 65 amnestic MCI and 60 age-matched controls were included in the study undergoing fMRI (3 Tesla ,TRIO, Siemens, Germany) and resting EEG-recordings (NeuroScan Synamps System). Current source density distributions were estimated using eLORETA Coherences between regions of interest, based on fMRI activation patterns were calculated.
Results: There were statistically significant differences between AD and aMCI for theta coherences between anterior cingulate gyrus (ACC) and left temporal gyrus (AD<aMCI, p<0.05); between AD and controls for theta coherence between ACC and right temporal gyrus (AD<

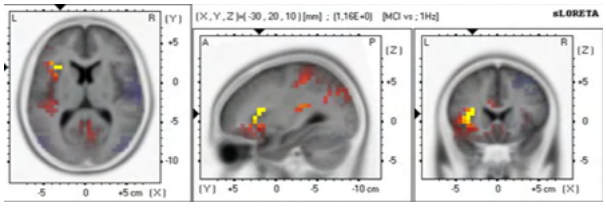
controls, p<0.01), ACC and left hippocampus (AD< controls, p<0.01), ACC and right parietal gyrus (AD<0.05). Theta coherence was lower in patients with aMCI compared with controls between anterior and posterior cingulate gyrus, (aMCI<controls, p<0.01), and between right and left temporal gyri (aMCI<controls, p<0.05).



Comparison of healthy elderly subjects vs. MCI patients. EEG-LORETA current source density activations. Correspondence in frontal, but not in posterior regions .



Comparison of healthy elderly subjects vs. AD patients. EEG-LORETA current source density activations. Correspondence in frontal, but not in posterior regions



Comparison of MCI and AD patients. EEG-LORETA current source density activations.Correspondence in posterior regions.

Conclusion: EEG coherence based on eLORETA could predict transformation from aMCI to AD.
Disclosure: Nothing to disclose.

EPO-197

Cognitive reserve moderates some changes induced by a dance intervention

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Background and aims: Dance is sensorimotor and cognitive activity providing positive effects for the elderly. Our previous research revealed positive behavioral effects of dance intervention (DI) on attention, executive function, and fitness in non-demented elderly. Here we explored whether DI-induced changes in functional connectivity (rsFC) of associated brain networks are moderated by cognitive reserve (CR).
Methods: 68 non-demented elderly were analyzed: 36 in the DI and 32 controls. All participants underwent cognitive and fitness testing and (f)MRI at baseline and six months after DI. Moderation analyses tested the effect of the CR (moderator, years of education-YoE) on the relationship between the program and change in the rs-FC of the sensorimotor network (SMN) and in the cross-talk between the dorsal attention network and the anterior part of the default mode network (DAN-aDMN).
Results: The SMN and the DAN-aDMN rs-FC increased in the DI group relative to the control, only the SMN rs-FC change depended on CR t(64)=3.20; p=0.02. SMN changed (p< 0.05) after the DI in high CR (YoE 15), no change was observed in moderate-to-low CR. No main effects was significant, only the interaction. DAN-aDMN rs-FC changes were dependent only on the main effect of the program t(64)=2.16; p=0.03.
Conclusion: The DI-induced increase of rs-FC of the SMN engaged in movement execution is dependent on high CR. This shows that the CR is linked to differing ability to benefit from DI. Intercommunication of age-sensitive neural node of CR, the DAN-aDMN, can be modulated by DI.
Disclosure: Nothing to disclose.

EPO-198

Mortality from Alzheimer's disease in Brazil: notifications from 2010 to 2019

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Background and aims: Alzheimer's disease is a group of brain disorders that cause the loss of intellectual and social skills. This study aimed to describe the evolution and characteristics related to mortality from the disease in Brazil.
Methods: An ecological study was carried out in January 2021 from the health information of the Brazilian Health Unified System databases. The analysis comprised the number of notified cases in Brazil from 2010 to 2019. The main variables analyzed were: sex, age, education, marital status, and region of notification. Descriptive statistics were performed through absolute (n) and relative (%) frequencies.
Results: Of the deaths from neurological diseases, Alzheimer's represents 48.48% of the total, accounting for 164,967 deaths. In the period analyzed, there was an increase from 10,814 in 2010 to 23,150 deaths in 2019. Most patients were female (64%), aged 80 or over (75%), One to three years of schooling (29%), and widowers (50%). In the distribution by region of the country, it was observed that 55% of the total occurred in the Southeast, 20% in the South, 17% in the Northeast, 5% in the Midwest, and 2% in the North.
Conclusion: Alzheimer's disease represents the largest contributor to mortality from diseases of the nervous system, standing out also for the increasing evolution of deaths. Therefore, it is necessary to invest in actions for screening and early diagnosis of this disease, to improve care assistance and quality of life for the population.
Disclosure: No disclosures.

EPO-199

Effectiveness of coping mechanisms used by caregivers of people with Multiple Sclerosis in reducing the disease burden

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Background and aims: Multiple sclerosis (MS) is one of the leading causes of neurological disability in young adults. Caring for people with MS (PwMS) is a stressful situation that can affect the quality of life of caregivers. This study aimed to sort the coping mechanisms used by caregivers of PwMS according to their effectiveness.
Methods: A cross-sectional survey of caregivers of PwMS recruited from Razi hospital MS Center was conducted between October and December 2020. Coping styles have been assessed based on the Tunisian version of the brief-Cope scale. The Hospital Anxiety and Depression Scale (HADS) was used to assess caregiver depression and anxiety.
Results: We included 51 caregivers of 46 PwMS. Mean EDSS of MS patients was 3.7. Caregivers were: 35% one of the parents, 31% the spouse, 25% one of the siblings and 7% one of the offspring. Half of them had depression and/or anxiety. The EDSS rate in PwMS was positively correlated to depression in caregivers (p=0.005). Approach coping styles (especially acceptance and planning) were more frequently used than avoidant coping styles (especially substance use and denial) (34.7% versus 23%) and inversely correlated with depression and anxiety in caregivers of PwMS (p=0.005). In contrast, avoidant coping mechanisms were significantly associated to a higher depression and anxiety rate.
Conclusion: Our study confirmed the effectiveness of the coping mechanisms approach in caregivers of PwMS to reduce disease burden. Health care professionals, specialized in MS, should recognize their difficulties and provide supportive strategies individualized to their specific needs.
Disclosure: Nothing to disclose.

Cerebrovascular diseases 2

EPO-200

Post-stroke Anxiety and Depression: a systematic review

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Background and aims: Major depressive disorder (MDD) and anxiety are relevant consequences of stroke and may influence the outcome of rehabilitation. Therefore, we aimed to investigate the relationship between these mood disorders and cerebrovascular accident.
Methods: This study is a systematic bibliographic review based on specialized literature, through the consultation of scientific articles selected in the PubMed, Scielo, and Cochrane databases. The descriptors "cerebrovascular accident" or "stroke" and "depressive symptoms" and "anxiety" were used for the search. The inclusion criteria were to find studies from the last five years that correlate MDD and/or anxiety with post-stroke events.
Results: A total of 14 studies were included. Mood disorders might be present in both acute or chronic phase of stroke and the number of cases found in each article may vary according to demographic factors, the scale used for diagnosis, exclusion criteria used by each study, and the time of assessment. Studies show that a patient's post-stroke neuroimaging correlates brain injuries with both the onset and severity of depression and anxiety. One of the studies showed that lesions in the right Rolandic operculum are associated with a worse psychological condition. However, there is no consensus on whether these findings are a direct consequence of the damage or if the physical-cognitive impairments produced by the lesion are the true cause.
Conclusion: The current study suggests that both the identification of specific injuries and appropriate screening for depression and anxiety may help to establish personalized rehabilitation plans.
Disclosure: The authors declare that there is no conflict of interests and the study did not receive financial support by any institution.

EPO-201

Stroke as the presenting manifestation of cardiac amyloidosis: a case report

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Background and aims: Ischemic stroke is a rare presentation of cardiac amyloidosis (CA) and is considered a marker for worse prognosis. The underlying mechanisms of thromboembolism in CA are thought to be multifactorial.
Methods: Case report
Results: An 80-year-old man presented to the emergency department with a newly onset motor deficit noticed upon waking. He had a past medical history of type-2 diabetes mellitus and hyperlipidemia. Physical examination revealed moderate dysarthria, left central facial palsy and left mild hemiparesis (NIHSS=5). Brain computed tomography (CT) scan showed a right insular hypodense area, and the CT angiography identified a distal occlusion to the right middle cerebral artery. He was started on dual antiplatelet and high-intensity statin therapy with clinical improvement. His blood analysis, including HIV and VDRL, were unremarkable. The electrocardiography identified sinus arrhythmia with no other clinically relevant events recorded during 48h monitoring. Transthoracic echocardiogram showed a left ventricle ejection fraction of 45% with myocardial deformation in an "apical sparing" pattern and elevated filling pressures, suggestive of an infiltrative cardiomyopathy. Cardiac magnetic resonance and cardiac scintigraphy later confirmed the diagnosis of cardiac amyloidosis and the patient is waiting for genetic testing for transthyretin mutations.
Conclusion: Amyloid fiber infiltration of the myocardium may lead to mechanical dysfunction and atrial thrombus formation, even with normal sinus rhythm. There are no formal guidelines addressing anticoagulation in CA without atrial fibrillation, and further studies are needed. CA awareness is important, especially in the Portuguese population, known for a high prevalence of transthyretin familial amyloid polyneuropathy.
Disclosure: No disclosures.

EPO-202

Association of cerebral microbleeds and neutrophil to lymphocyte ratio in acute ishemic stroke patients

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Background and aims: Brain parenchymal changes on conventional magnetic resonance imaging (MRI) are indirect markers of cerebral small vessel disease (SVD) and include recent small subcortical infarcts, white matter hyperintensities, lacunes, prominent perivascular spaces, cerebral microbleeds (CMB), and atrophy. Elevated neutrophil to lymphocyte ratio (NLR), a simple marker of systemic inflammation, has been used as a predictor of poor prognosis in ischemic stroke patients with large vessel occlusions. However, association between NLR and SVD is controversial. Here, we aimed to investigate whether there is an association between CMB load, a marker of SVD in brain, and NLR in acute ischemic stroke patients.
Methods: We performed a retrospective cohort analysis of consecutive acute ischemic stroke patients admitted within seven days of symptom onset. We reviewed the medical records and laboratory test results on admission. Brain MRIs performed on admission were evaluated for white matter hyperintensities on T2 weighted images, acute infarct locations on diffusion weighted images and CMB number and locations on susceptibility weighted images.
Results: We enrolled 127 patients with acute ischemic stroke. Cerebral microbleeds were detected in 37 percent (n=47) of patients. Among demographic features and cardiovascular risk factors, patient's age was the only predictor of CMB number. CMB number significantly correlated with leukoaraiosis severity indicated by Fazekas score. NLR was not found to be associated with CMB load.
Conclusion: Our study demonstrated characteristics and correlations of SVD in acute stroke patients. An inflammatory marker, NLR, failed to correlate with CMB, at least in acute setting of ischemic stroke.
Disclosure: No disclosures.

EPO-203

Extracellular vesicles from hypoxia-conditioned microglia are protective in stroke mice via the TGF-/Smad2/3 pathway

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Background and aims: Transplantation of oxygen-glucose-deprivation (OGD)-conditioned microglia enhances neurological recovery in stroke. Herein, we analyzed if extracellular vesicles (EVs) from such microglia are the biological mediators of this process.
Methods: EVs were harvested from microglia exposed to OGD followed by a characterization using Western blotting, nanoparticle tracking analysis (NTA), and transmission electron microscopy (TEM). These EVs were used in in vitro and in vivo stroke models. Immunohistochemistry, flow cytometry analysis, and behavioral tests were done during the observation period of seven days poststroke.
Results: Characterization of EVs from OGD-conditioned microglia displayed the expression of typical EV markers and presented an EV-like phenotype in the TEM analysis. Such harvested EVs were found to be highly enriched in TGF-1. Interfering with the latter by means of knockdown experiments or by inhibiting the TGF-1 receptor reversed various effects observed due to EV application under both in vitro and in vivo conditions. These observations include an activation of the SMAD2/3 pathway in endothelial cells and neurons exposed to hypoxia as well as in stroke mice. Along with activating this signaling pathway is a stimulation of angiogenesis and a reduction of cell injury under in vitro and in vivo settings. Injection of EVs into stroke mice drove residential microglia into the anti-inflammatory M2 state, contributing to the aforementioned effects and to a better neurological recovery.
Conclusion: EVs derived from OGD-conditioned microglia promote neuroprotection, tissue regeneration, and neurological recovery in a TGF-1-dependent manner. These results further underline the great therapeutic potential of EVs for future stroke treatment.
Disclosure: Nothing to disclose.

EPO-204

Clinico-radiological profile and treatment outcomes of patients with ischemic stroke in a tertiary care centre in India

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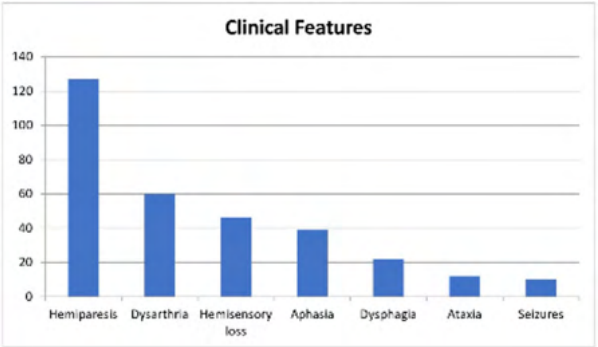
Background and aims: Cerebrovascular diseases are major causes of mortality and disease in the Indian subcontinent. Presenting clinical features and findings, time of onset and time taken to seek health care and treatment modalities available, directly or indirectly affects the outcome of stroke.
Methods: A prospective observational study was conducted amongst patients admitted in the department of Neurology and Medicine between October 2018 to October 2019. All patients above the age of 15 years, who presented with clinical features suggestive of acute stroke, were subjected to CT scan of brain and total 150 patients with evidence of acute ischemic infarct were included.
Results: The mean age of participants was 56 ±13.6 years. Hemiparesis was the most common presentation seen in 127 (84.67%) patients, with left hemiparesis present in 86 (57.33%) of them. Dysarthria and aphasia were noted in 60 (41.33%) and 39 (26%) patients respectively. Hypertension was present as a major risk factor in 102 (68%) and Diabetes in 62 (41.33%) of patients. Total seven (4.67%) of patients reached the hospital within three hours of onset of stroke. Middle Cerebral Artery was the most commonly involved in 113 (75.33%) patients. 93 (62%) of patients had mild to moderate stroke (mRS grading). Mortality rate was 6% on the tenth day of stroke onset.



Clinical Features

Conclusion: Ischemic stroke constitutes a significant cause of mortality in India. The less proportion of patients reaching hospitals within three hours of stroke in turn impacts the outcome of the disease and increases stroke related mortality and morbidity.
Disclosure: Nothing to disclose.

EPO-205

Post stroke depression: prevalence and associated factors in a Tunisian cohort

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[1] Neurology Departement CHU Sahloul, Sousse, Tunisia, [2] Neurology, Sahloul, Tunisia

Background and aims: Poststroke depression (PSD) is prevalent and is an important determinant of functional recovery, quality of life and mortality after stroke. Scanty data on the nature of PSD among stroke survivors in Tunisia prompted this study. Our aim was to investigate the prevalence of depression and its associated factors among patients suffered from stroke, in a Tunisian hospital.
Methods: This cross-sectional study was carried out among patients suffering from acute stroke in neurology department in Sahloul Hospital over a period of one year. Participants were administered questionnaires to profile their socio-demographic and clinical characteristics. Subsequently, they were assessed with the Montreal Cognitive Assessment (MoCA), Beck Depression Inventory (IDB) and NIHSS at one week and at three months.
Results: 142 patients were included. The mean age was 65 years. The sex ratio was 1.68. PSD prevalence was 57% initially and 51.1% at three months. We found significant correlations between PSD at one week and HTA (p=0.003) and stroke severity assessed by NIHSS (p=0.012). However PSD at three months were significantly associated with sex (p=0.004), marital status (p=0.04), physical disability (p=0.001) and cognitive impairment (p=0.021).
Conclusion: Findings in this study support the need to focus on moods disorders post stroke. Early rehabilitation and psychological interventions targeting people with not modifiable related factors are needed to improve well-being.
Disclosure: Nothing to disclose.

EPO-206

CADASIL – which characteristics are good predictors in a hospital-based cohort?

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Background and aims: Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is a genetic arteriopathy caused by Notch3 mutations. Patients may present migraine with aura, lacunar stroke or cognitive decline. Recently, the European Academy of Neurology published consensus recommendations regarding its diagnosis and treatment. Our aim was to apply these criteria to our patients with suspected genetic small-vessel disease to determine the sensitivity and specificity of these guidelines.
Methods: We collected data from patients followed at our center due to suspected genetic small-vessel disease who underwent genetic testing for Notch3 pathogenic variants, including history of migraine with aura, stroke, early onset dementia and characteristic MRI imaging changes.
Results: 49 patients were evaluated. 21 presented Notch3 mutation, 28 showed no mutation. 10 patients had a familial history of CADASIL, 12 were index cases. Mean age of diagnosis was 53 years. Patients with Notch3 variants had more frequently history of early onset dementia (23% vs 3.5%, p=0.032), migraine (45 vs 10.7%, p=0.007), migraine with aura (25% vs 3.8%, p=0.031) and temporal pole hyperintensities on MRI (50% vs 21%, p=0.44). Both groups did not differ in gender, family history of epilepsy or young-onset stroke, age of first stroke, prevalence of headache or migraine. In our population, the recommendations showed a 94% sensitivity and a 53% specificity.
Conclusion: Only early-onset dementia, migraine with aura and temporal lobe changes were correlated with the presence of Notch3 mutation. The consensus recommendation showed high sensitivity and a reasonable specificity for diagnosing CADASIL in our cohort.
Disclosure: The authors have nothing to disclose.

EPO-207

The NLRP3-inflammasome as key player in "thrombo-inflammation" during cererbral ischemia

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Background and aims: Ischemic Stroke (IS) causes harm to the affected brain tissue not solely due to insufficient blood supply during vessel occlusion but also because of neuroinflammatory responses. Despite successful recanalization, infarcts frequently continue to grow based on additional inflammatory processes. Inflammasomes, intracellular multi-protein complexes, have recently been described as being involved in various systemic inflammatory diseases as exemplarily arteriosclerosis. To elucidate the inflammasomes' role in the cerebral postischemic neuroinflammatory processes we studied the effect of inflammasome inhibition in mice anticipating a reduction of thrombo-inflammation and an improved outcome.
Methods: We induced focal cerebral ischemia in WT-mice by 60min transient middle cerebral artery occlusion (tMCAO). Animals were treated with three inflammasome-inhibitors of different specificity or vehicle before/after tMCAO. Stroke outcome, including infarct size, functional deficits and the local inflammatory response, was assessed on day one after tMCAO.
Results: Inflammasome inhibition significantly reduced stroke volumes. Concurrently the intracerebral immune cell accumulation decreased and the neuronal density augmented in mice treated with inflammasome inhibitors. The BBB-integrity was stronger in treated than in control mice. Moreover, treated mice performed significantly better in neurologic tests after tMCAO in comparison to vehicle. With regard to the inflammasome-subtypes themselves we could depict an increase of NLRP3-gene expression and a primarily neuronal upregulation of NLRP3 after IS while the other inflammasomes showed lesser or no regulation.
Conclusion: NLRP3 is a key player in thrombo-inflammation. Targeting this molecule may become a promising therapeutic strategy in acute IS, without affecting the hemostasis of the ischemic brain, which is susceptible to bleeding complications.
Disclosure: Nothing to disclose.

EPO-208

N-Terminal-pro-B-type-Natriuretic-Peptide for the diagnosis of cardioembolic ischemic stroke

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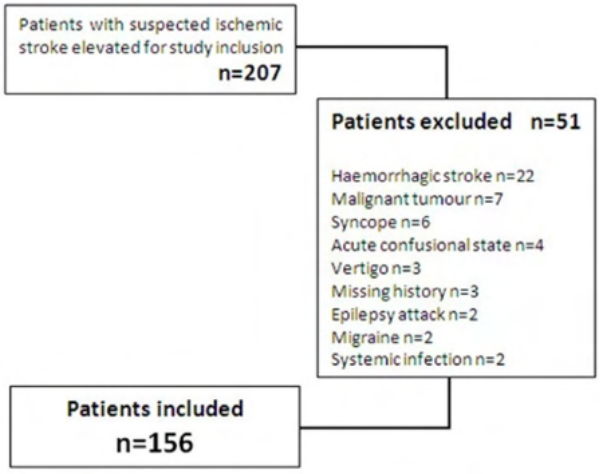
Background and aims: Despite a complete and exhaustive study, the origin of 35% of ischaemic strokes is unknown. We aimed to assess the diagnostic ability of NT-proBNP for the identification of ischemic stroke of cardioembolic origin. The secondary purpose was to evaluate the prognostic value of NT-proBNP for predicting 90-days all-cause mortality.

Methods: This is a prospective observational study including adult patients hospitalized by stroke. The recruitment period was from March 2019 to March 2020. Blood samples were obtained on admission and serum NT-proBNP levels were measured by an electrochemiluminescence immunoassay. Statistical analysis were performed by using the bivariate logistic regression model, the receiver operating characteristic (ROC) and Kaplan-Meier curves. Statistical significance was set at $p<0.05$.



Results: 207 patients with first ischemic stroke were included. NT-proBNP plasma levels were significantly increased ($p<0.001$) in the cardioembolic stroke group (2,069±488.5). ROC curves showed that NT-proBNP>499 pg/mL was the optimum value for the diagnosis of ischemic cardioembolic stroke (sensitivity 82%, specificity 80%). Moreover, NT-proBNP>499pg/mL plasma levels were independently associated to cardioembolic stroke (OR=9.881, p=0.001). Finally, NT-proBNP>1,500pg/mL was useful to predict mortality at 90 days post-stroke (sensitivity=70%, specificity=93%).

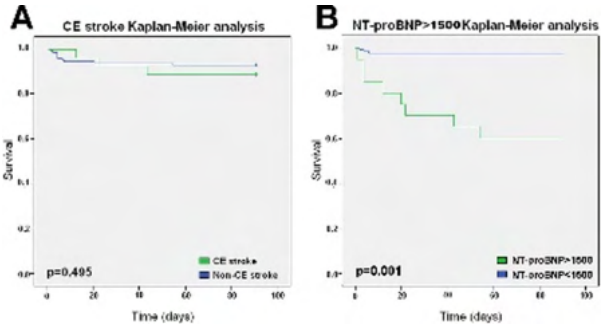


Table 3. Non-cardioembolic vs. Cardioembolic stroke by bivariate logistic regression model

	OR	IC95%	*p*-value
Age	0.999	0.949-1.055	0.986
DM	4.550	0.870-23.683	0.072
AF/valve/shunt	0.395	0.126-1.237	0.111
Tobacco	5.866	0.598-57.575	0.129
LDL	0.998	0.985-1.011	0.768
NT-proBNP	1.001	1.000-1.002	**0.003**
NT-proBNP>499	9.881	2.831-34.489	**0.001**

Abv: DM=diabetes mellitus; AF=atrial fibrillation; LDL=low density lipoprotein; NT-proBNP=N-terminal-pro brain derived natriuretic peptide.

Conclusion: NT-proBNP was independently associated to cardioembolic stroke and should be considered for blood testing within 24h of stroke. High plasma levels (NT-proBNP>499pg/mL) may indicate an underlying cardiac cause which should be further studied while NT-proBNP>1,500pg/mL was associated with increased mortality after 90 days.

Disclosure: Funding: The Authors neither received public or private funding nor grant to carry out this study. Conflict of interests: The Authors declare that there is no conflict of interest.

EPO-209

Clinical and evolutionary profile of patients with ischemic stroke caused by cervico-cephalic arterial dissection (CAD)

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Background and aims: Cervico-cranial arterial dissections, recognized by the presence of a hematoma within the arterial wall, are a distinct etiology of neurovascular events, including acute ischemic stroke and transient ischemic attack, as well as subarachnoid hemorrhage. Cervical artery dissection is suspected clinically and confirmed by neuroimaging techniques including magnetic resonance imaging, computerized tomographic angiography and conventional angiography.

Methods: We retrospectively reviewed the medical charts and neuroimages of patients who are hospitalized at the neuro-vascular unit of the Neurology Department at the Sahloul University Hospital in Sousse for acute ischemic stroke secondary to a cervico-encephalic dissection from 2015 to 2020. We reviewed demographical, clinical and neuroimaging data and recorded hemorrhagic complications, NIHSS at discharge mortality within seven days and modified Rankin Scale at 3-months. All the information was analyzed using SPSS 20 software to calculate percentages, medians and means. No ethical problem has arisen.

Results: 16 patients were included. Median age was 52 years. The sex ratio M/F was 1.5. Hypertension was the most frequent vascular risk factors. The initial examination found motor deficit in nine patients, aphasia in two patients, visual disturbances in four patients, cerebellar syndrome in five patients. 14 patients were started on antiplatelet therapy. Only two patients were put on anticoagulant. One patient died within seven days from ischemic mass effect. After three months, five patients had favorable clinical outcomes.

Conclusion: Ischemic strokes secondary to CAD are as common in the elderly as in young people. Their diagnosis is based on imaging which should be done as soon as possible.

Disclosure: Nothing to disclose.

EPO-210

Swallowing disorders in post-stroke patients

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Background and aims: Swallowing disorders(SD) are a prevalent poststroke condition. They have been associated with complications such as malnutrition and respiratory infections which lead to poor prognosis and high mortality. The aim of our study was to evaluate the prevalence of SD after stroke, the risk factors and associated complications.

Methods: We performed a prospective study of stroke patients consecutively admitted to our department. SD was diagnosed with the Eating Attitude Test (EAT-10 test 2). Demographic, topographical and clinical variables of stroke were collected to assess risk factors for SD. We evaluated functional status (MRS, Barthel score) three months after stroke.

Results: We included 50 stroke patients with a 64% prevalence of SD. The mean age was 65±12.77 years with a sex ratio (F/M)=2/3. The mean EAT-10 score was 4.14 ±4.5. Stroke was ischemic in 86 % and hemorrhagic in 14%. The mean of the initial NIHSS was 5.3±3.4. SD were associated with dysarthria ($p=0.01$), hemorrhagic stroke ($p=0.049$) and increased initial NIHSS ($p<0.001$). SD was at risk factor for poorer functional capacity according to MRS ($p=0.005$) and Barthel scores ($p=0.07$).

Conclusion: Poststroke SD is prevalent and associated with poor short term prognosis. Stroke severity, dysarthria and the hemorrhagic type of stroke were more relevant to SD than lesion location. Systematic screening programs and early SD management could significantly improve poststroke patient outcome.

Disclosure: The authors do not disclose any conflict of interest.

EPO-211

Stroke as part of the clinical spectrum of KILT syndrome: first case described

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Background and aims: The recently described KILT syndrome consists of the association of deep venous thrombosis with inferior vena cava abnormalities and renal defects. Only fifteen cases have been reported, most of them young patients with a clinical presentation of abdominal pain and swelled legs and without a burden of thrombotic or immunological factors. No neurological involvement due to arterial infarction had been described.

Methods: We report for the first time a patient diagnosed with KILT syndrome with a clinical atypical presentation of epileptic ictal phenomena due to strokes in multiple territories.

Results: We discuss about the case of a 33-year-old male with a previous diagnosis of KILT syndrome presenting a new clinical picture of confusion with normal neurological exploration. Cranial magnetic resonance imaging (MRI) showed findings compatible with subacute left frontal stroke along with multiple bihemispheric cortical and subcortical punctate foci with restriction on diffusion-weighted sequences indicating more recently strokes on different territories. There were no signs of sinus venous thrombosis. Radiologically, these lesions suggest co-existing risk factors such as coagulopathy or either cardioembolic source although no evidence of them were found. Nevertheless, extensive hematologic and immunologic workup was unremarkable and no evidence of shunt on echocardiogram and by bubble test on transcranial Doppler ultrasound was found. The patient was discharged asymptomatic and on treatment with apixaban.

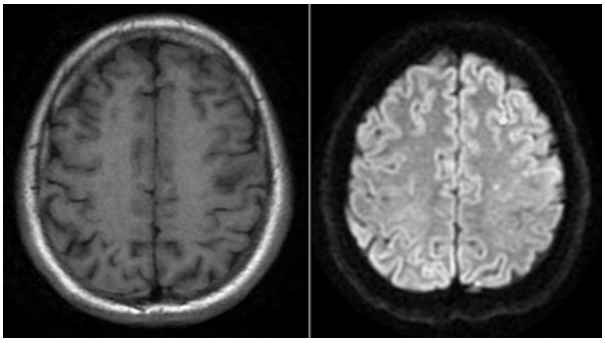

Fig. 1. A. MRI FLAIR-weighted imaging without restriction in diffusion-weighted (DW) sequence showed a subacute/chronic ischemic lesion on left precentral gyrus. B. In DW images, multiple hyperintense punctate foci with decrement on apparent diffusion coe

Conclusion: Although KILT syndrome have been almost exclusively related to venous thrombosis, might also produce arterial thrombotic events. We hypothesized that unknown associated etiopathogenic mechanisms might be involved.

Disclosure: Authors declare no conflict of interests.

EPO-212

Impact of moon phases in pacients with no-traumatic intracerebral hemorrhage

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Background and aims: Stroke and intracerebral hemorrhage (ICH) occurrence shows strong correlations with sleep disorders. Lunar cycles have also been shown to affect sleep and other physiological processes, but studies on moon phases and their possible association with neurovascular events are rare and nonconclusive. The aim of this work was to study the effects of moon phases on ICH.
Methods: We retrospectively reviewed the discharge registry data of all patients with ICH diagnosis admitted to our Hospital between May 2017–May 2020. We collected variables such as date of admission, moon phase, the season of the year or mortality. The onset times of ICH were assigned to four primary lunar phases based on NASA definitions. We used the R Studio v4.0.3 to perform the statistical analysis.
Results: 103 cases of ICH were found. 67% were males and the median age at diagnosis was 69 years (range 37–84). 22% of ICH happened on full moon, 23% on waining, 26% on new y 28% on crescent. There was no association between moon phase and Intracerebral Hemorrhage occurrence in our patients. There were no differences between moon phases neither in daily admission nor in mortality rates among different subgroups (sex and age). No significant interactions between moon phase and astronomical season for stroke occurrence were found.
Conclusion: In our study, we found no association between moon phases and occurrence or mortality of ICH. Some previous studies have investigated the association between lunar phase and stroke, but the findings have been conflicting, specifically in non-traumatic ICH where no relationship has ever been described.
Disclosure: The authors declare no conflicts of interest.

EPO-213

Isolated Cortical Vein Thrombosis: don't bet it all on the CT venography!

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Background and aims: Isolated cortical vein thrombosis (ICVT) is a rare entity, frequently resulting in parenchymal brain injury (localized oedema, intracerebral haemorrhage and/or venous infarction). Therefore, early recognition and prompt treatment are crucial. Considering that the clinical manifestations are often nonspecific, imaging plays a key role in establishing an accurate diagnosis.
Results: A 35-year-old puerperal female patient presented with acute persistent headache and left upper extremity weakness, numbness and involuntary movements (brief, without impairment of consciousness). Neurological examination revealed left central facial palsy, as well as mild paresis, distal hypoesthesia/hypopalesthesia and sensory ataxia of the left upper extremity. Head CT showed a right perirolandic cortical-subcortical lesion, heterogeneous, with oedema and petechial haemorrhages. CT venography was described as normal. However, subsequent brain MRI with venography documented isolated thrombosis of the right parietal cortical vein. The EEG did not show epileptic activity. A diagnosis of ICVT complicated by venous infarction (with haemorrhagic transformation) and symptomatic epilepsy (focal, without impairment of consciousness) was established. Both anticoagulation and antiepileptic treatment were initiated, with favourable outcome. Further investigation uncovered sickle cell trait and iron-deficiency anaemia, with the remainder being normal or negative.
Conclusion: ICVT may present with nonspecific clinical manifestations, and even with normal CT scan and/or CT venography. Our case illustrates the need of enforcing urgent brain MRI with venography when clinical suspicion is high, even when confronted with a normal CT venography. Besides the puerperium, the sickle cell trait should be regarded and managed as a thrombotic risk factor, especially in future pregnancies.
Disclosure: Nothing to disclose.

EPO-214

New remote cerebral microbleeds on T2*-Weighted Echo Planar MRI after intravenous thrombolysis for acute ischemic stroke

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Background and aims: The risk of recombinant tissue plasminogen activator (rtPA)-related cerebral microheamorrhages in acute ischemic stroke (AIS) is unknown. We investigated the frequency of new cerebral microbleeds (CMBs) after intravenous thrombolysis (IVT), and their associations with data on haemorrhagic transformation and clinical characteristics in AIS patients.
Methods: Fifty-nine consecutive patients with AIS, treated with rtPA underwent MRI including T2*-Weighted Echo Planar Imaging before and seven days after rtPA administration. We considered only those new CMBs that were located outside the MR diffusion restriction area, and investigated the associations between their occurrence and presence of heamorrhagic transformation in neuroimaging along with clinical characteristics, using multivariate logistic regression analysis.
Results: 49 patients were included for the final analysis. On initial T2*-EPI, 37 baseline CMBs were observed in 14 patients (28.6%). On follow-up T2*-EPI, new CMBs were found in five (14.3%) of 35 patients without and in nine (64.3%) of 14 with any baseline CMBs. 48 (72.7%) new CMBs were localized in cortical/subcortical area, and 18 (27.3%) in deep brain structures. Multiple logistic regression analysis indicated that presence of baseline CMBs (OR 5.95, 95% CI 2.69–13.20, p<0.001) and platelets level (OR 0.992, 95% CI 0.986–0.998, p=0.007) were independently associated with new CMBs. New CMBs were not associated with the risk of heamorrhagic transformation.
Conclusion: Pre-IVT CMBs do not increase the risk of heamorrhagic transformation but might augment the risk of new rtPA-related CMBs. However, the clinical significance of the latter remains to be investigated.

	1 (N=14)	0 (N=35)	Total (N=49)	p value
Age				**0.026**
Mean (SD)	74.1 (10.9)	62.1 (18.2)	65.5 (17.2)	
Median (Q1,Q3)	72.5 (66.5, 84.0)	67.0 (46.0, 75.5)	66.0 (56.0, 80.0)	
Gender: Male	8 (57.1%)	15 (42.9%)	23 (46.9%)	0.765
Time from onset to treatment, min				0.734
Mean (SD)	177.4 (63.3)	170.9 (59.5)	172.8 (60.0)	
Median (Q1,Q3)	175.0 (131.2, 226.0)	171.0 (120.5, 215.0)	171.0 (130.0, 220.0)	
Hypertension	13 (92.9%)	27 (77.1%)	40 (81.6%)	0.419*
Diabetes	6 (42.9%)	11 (31.4%)	17 (34.7%)	0.448
Antiplatelet drugs	5 (35.7%)	15 (42.9%)	20 (40.8%)	0.646
Systolic blood pressure admission, mmHg				0.226
Median (Q1,Q3)	160.5 (152.2, 178.2)	148.0 (138.0, 174.5)	150.0 (139.0, 176.0)	
Diastolic blood pressure admission, mmHg				0.679
Median (Q1,Q3)	87.0 (74.0, 90.8)	83.0 (74.0, 92.0)	83.0 (74.0, 92.0)	
Glucose, mg/dl				0.715**
Median (Q1,Q3)	126.0 (104.5, 141.2)	121.0 (105.0, 142.0)	121.0 (104.0, 143.0)	
Leukocytes, k/ul				0.250**
Median (Q1,Q3)	6.3 (5.9, 9.2)	8.0 (6.7, 9.3)	7.5 (6.2, 9.4)	
Platelets, x10^9/l				0.250**
Median (Q1,Q3)	222.0 (182.5, 240.8)	234.0 (192.5, 291.5)	231.0 (182.0, 266.0)	
Creatinine, mg/dl				**0.035**
Mean (SD)	1.0 (0.2)	0.9 (0.2)	0.9 (0.2)	
Median (Q1,Q3)	1.0 (0.9, 1.1)	0.8 (0.7, 0.9)	0.9 (0.7, 1.0)	
INR				0.827
Mean (SD)	1.0 (0.1)	1.0 (0.1)	1.0 (0.1)	
Median (Q1,Q3)	1.0 (0.9, 1.0)	1.0 (0.9, 1.0)	1.0 (0.9, 1.0)	
NIHSS admission				0.600**
Median (Q1,Q3)	5.0 (1.0, 5.8)	5.0 (3.0, 10.0)	5.0 (3.0, 7.0)	
Hemorrhagic transformation ECASS				0.147*
HI1	3 (21.4%)	3 (8.6%)	6 (12.2%)	
HI2	1 (7.1%)	1 (2.9%)	2 (4.1%)	
PH1	0 (0.0%)	1 (2.9%)	1 (2.0%)	
PH2	0 (0.0%)	1 (2.9%)	1 (2.0%)	
Baseline DWI Volume, ml				0.165**
Median (Q1,Q3)	0.0 (0.0, 0.0)	0.0 (0.0, 14.5)	0.0 (0.0, 9.0)	
Presence of baseline CMBs	9 (64.3%)	5 (14.3%)	14 (28.6%)	**<0.001**
SVD, 2-3	5 (35.7%)	8 (22.9%)	13 (26.5%)	0.357

SD: standard deviation, Q1: the first quartile, Q3: the third quartile, fe: Fisher's exact test, m-w: Mann-Whitney test.

The clinical and neuroimaging characteristics of participants with and without new CMBs

Disclosure: Neuroimaging studies founder is Siemens Healthcare (Siemens Healthineers).

Cognitive neurology/neuropsychology 1

EPO-215

Longitudinal evaluation of eye movements in mild cognitive impairment

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Background and aims: This study aims to evaluate longitudinal changes in saccadic eye movements in mild cognitive impairment (MCI).
Methods: Over a period of two years we studied longitudinally three groups: 12 amnestic mild cognitive impairment patients (aMCI), seven non-amnestic mild cognitive impairment patients (naMCI) and 15 healthy controls (HCs) matched for age and education. We measured their cognitive function and their saccadic eye movements: horizontal and vertical pro-saccades and horizontal anti-saccades.
Results: During the period of the study: (a) Mini-Mental State Examination (MMSE) score decreased significantly in both aMCI and naMCI (p=0.05). (b) three aMCI patients progressed to Alzheimer's disease and one HC progressed to naMCI; (c) Anti-saccade latency decreased significantly in aMCI but not in naMCI and increased in HCs (p=0.05). (d) Anti-saccade error rate showed significant negative correlation with changes in language in aMCI (p=0.011). (e) Anticipatory anti-saccade rate showed significant negative correlation with changes in executive function in HCs, (p= 0.023). (f) Horizontal but not vertical pro-saccade latency showed a significant negative correlation with changes in executive function in naMCI (p=0.042).
Conclusion: Decreased anti-saccade latencies in aMCI could show the variability of MCI whereas increased latencies in HCs may be a predictor of future cognitive dysfunction. Longitudinal follow-up more than two years might be needed to confirm the changes in the conditions studied. The relationship between anti-saccade error rate and language suggests that change in language skills may provide important results in future studies.
Disclosure: The authors report no conflicts of interest. All authors declared that they received no financial support.

EPO-216

2 cases of Corticobasal Degeneration Presenting as Non-Fluent Primary Progressive Aphasia

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Background and aims: Non-fluent primary progressive aphasia is characterized by progressive non-fluent speech disorder and might be associated with corticobasal degeneration (CBD) especially with certain features.
Methods: Two cases of Corticobasal Degeneration presenting as Non-Fluent Primary Progressive Aphasia are reported. The medical literature was reviewed.
Results: The first case was a 78-year-old right-handed man whose initial symptom was slowly progressive aphasia. Neurological examination revealed aphasia, dysexecutive syndrome and rigidity of the right upper extremity. Neuropsychological assessment disclosed Broca's aphasia and memory disturbance. MRI of the brain showed atrophy of the parietal lobes, which was more severe on the left. Brain scintigraphy showed asymmetric parietal low perfusion and of the basal ganglia. The second case was a 36-year-old man whose father was diagnosed frontotemporal dementia. He initially presented language impairment then memory loss then walking difficulties. His neurologic evaluation showed a dysexective syndrome, parkinsonian syndrome, upper limb dystonia of the right arm and non-fluent aphasia. MRI of the brain showed left parietal lobe atrophy. Brain scintigraphy showed left parietal lobe hypoperfusion. In most reported cases of CBD, the initial symptom is motor dysfunction of the unilateral upper extremity. However, we should be cautious that among cases with CBD, there have been rare cases that begin with progressive aphasia alone. In our cases, the atrophied region of the cerebral cortex was most severe around the parietal lobe.
Conclusion: Those cases suggest that CBD should be included in the differential diagnosis of primary progressive aphasia.
Disclosure: Not granted by any commercial or institutional support.

EPO-217

Transient Global Amnesia and the Venous Drainage Hypothesis

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Background and aims: Transient Global Amnesia (TGA) is a clinical syndrome characterized by acute onset anterograde amnesia, usually lasting a few hours. Its pathogenesis remains unclear. Venous congestion is one of the hypotheses. A potential trigger associated with TGA is a Valsalva-like maneuver, with increased pressure from chest and abdomen transmitted to the intracranial compartment via the epidural venous plexus or vertebral venous plexus. Orthograde internal jugular veins (IJ) venous outflow emerging shortly after Valsalva serve as a mechanism for regulating the intracranial pressure and equalizing the pressure within the venous system. A large arteriovenous malformation (AVM) may lead to a dysregulation of this adaptative mechanism and trigger this TGA presentation.
Methods: Case report and review of the literature.
Results: 46-year-old right-handed man was admitted for intraventricular hemorrhage (IVH) secondary to ruptured AVM, manifested by headaches, transient disorientation and acute anterograde amnesia that suddenly started while herding cattle. The episode lasted around five hours, with persistent amnesia of the episode afterward. His clinical exam at admission was non focal, with normal language and orientation. Imaging revealed a very large AVM involving most of the left parietal and occipital lobe associated with IVH in the left lateral ventricle and 4th ventricle, without hydrocephalus or midline shift. Computed tomography angiography and conventional angiography demonstrated deep venous drainage in addition to the large venous pouch draining in the superior sagittal sinus and left transverse sinus, without infarction.
Conclusion: This case report supports the venous congestion hypothesis in TGA pathogenesis, but studies on larger groups are needed.
Disclosure: Nothing to disclose.

EPO-218

Mocha coffee consumption correlates with cognitive function in a population with subcortical ischemic vascular disease

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Background and aims: To date, there are inconclusive evidences for a protective effect of coffee consumption on the occurrence and course of age-related neurological and neuropsychiatric disorders. Moreover, no study has been carried out in mild vascular cognitive impairment and late-life depression.
Methods: We assessed the association between different quantities of mocha coffee consumption over the last year on both cognitive and mood performance in a non-demented elderly Italian population with subcortical ischemic vascular disease (SIVD). The outcome measures were Mini Mental State Examination (MMSE), Stroop Color-Word Interference test (Stroop T), 17-items Hamilton Depression Rating Scale (HDRS), Activities of Daily Living (ADL), and Instrumental ADL scores.
Results: MMSE, HDRS, and Stroop T independently and significantly correlated with coffee consumption, i.e., better scores with increasing intake. Post-hoc analyses showed that the group with a moderate coffee intake (2 cups/day) had similar values compared to the heavily drinkers (3 cups/day), with the exception of MMSE score.

	Coffee 0 (n=73)		Coffee 1 (n=69)		Coffee 2 (n=87)		Coffee ≥3 (n=71)		ANOVA	
	mean	SD	mean	SD	mean	SD	mean	SD	$F_{3,294}$	$p <$
Age, years	73.9	6.2	72.9	5.7	73.5	6.4	70.9	5.6	3.623	0.014
Education, years	6.5	3.7	6.9	4.0	7.5	4.0	8.2	3.9	2.635	0.05
MMSE	25.9	1.8	25.5	1.6	25.9	1.9	26.8	2.1	6.212	0.00042
ADL	5.6	0.7	5.5	0.7	5.6	0.6	5.8	0.6	2.112	NS
IADL	7.2	1.3	6.8	1.5	7.1	1.2	7.3	1.2	1.814	NS
HDRS	11.7	6.4	8.7	6.0	5.8	4.8	5.1	3.6	23.790	0.000001
Stroop T	50.3	22.9	47.1	21.6	41.4	20.4	35.3	18.6	7.182	0.00011

Table 1. Comparison of continuous variables obtained from the four groups of subjects.

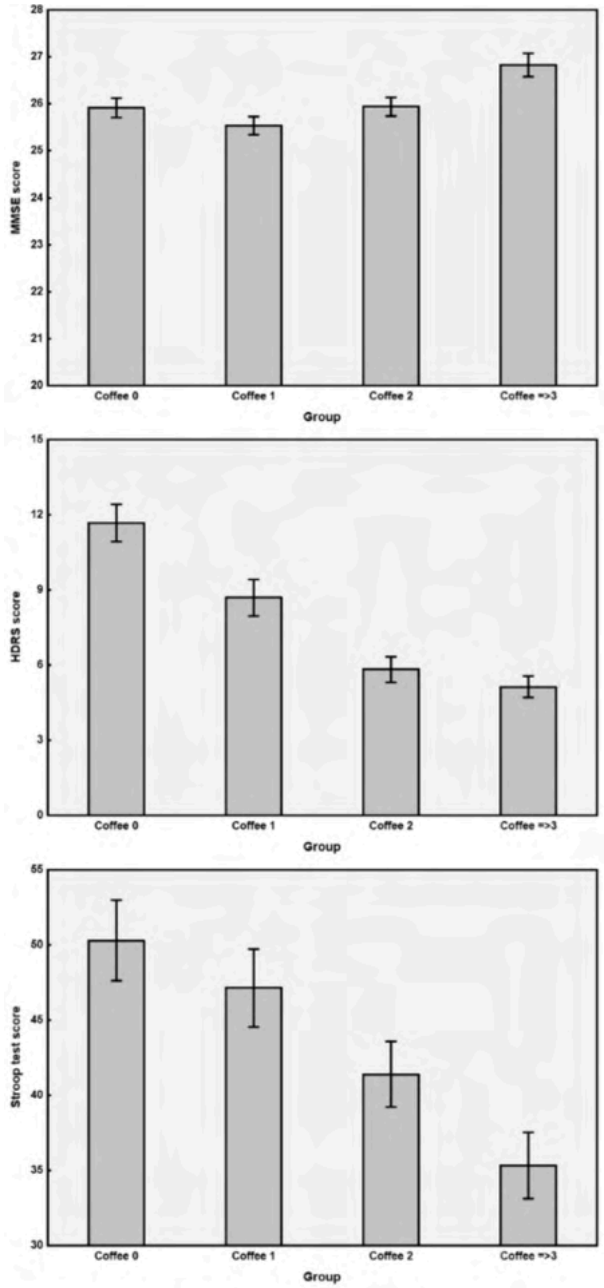

Figure 1. Histograms of continuous outcome variables obtained from the four groups of subjects and showing significant differences in Table 1.

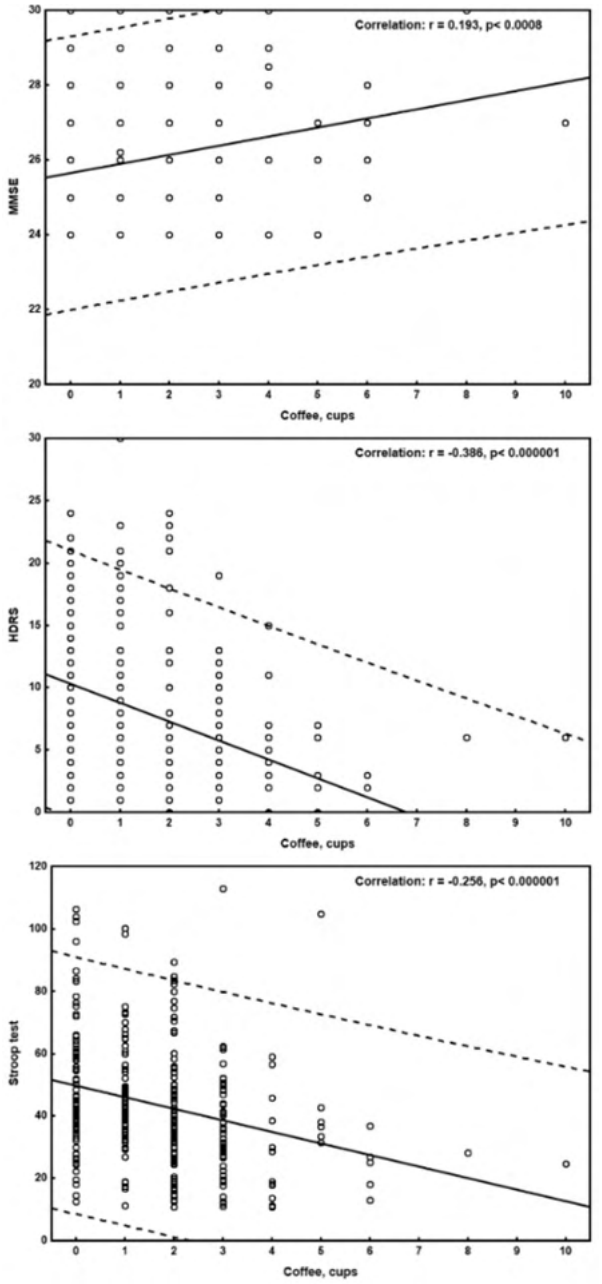

Figure 2. Regression analysis between the score obtained and the number of coffee cups consumed daily by the subjects.

Conclusion: Daily coffee consumption was associated with better cognitive performance and mood status, with a significant dose-response effect even with a moderate intake. These findings might have translational implications for the identification of modifiable factors for the occurrence and severity of vascular dementia and geriatric depression.
Disclosure: The authors declare no conflict of interest.

EPO-219

MAPT mutation frontotemporal dementia with parkinsonism: when previous results can skew the diagnosis

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Background and aims: In frontotemporal dementia with parkinsonism (FTDP), several mutations in MAPT gene have been identified, and numerous family cases were reported, since this mutation was first discovered.
Methods: Case report
Results: We present a 48-year-old, Caucasian woman with FTDP linked to the MAPT gene mutation (c.1842T>G (p. Asn614Lys)). Physical examination and neuropsychological assessment revealed a frontotemporal syndrome. Approximately one year later she developed a hypokinetic movement disorder and pyramidal signs. Brain MRI revealed mild frontotemporal atrophy. The history includes a pedigree with an autosomal dominant pattern of transmission. A patient's sibling with similar syndrome, investigated in 2000, had performed cerebral biopsy with neuropathological findings suggesting a tauopathy associated with a chromosome 17 mutation. Nevertheless, genetic analysis was negative, eliminating initially the attempt to diagnose the FTDP linked to mutation in MAPT, therefore other hypotheses were investigated, namely C9ORF72 among others. With the development of new generation sequencing (NGS) the association with MAPT gene was found.
Conclusion: An important pitfall avoidance option can be the frequent reevaluation of previous diagnosis in families, in which the clinical presentation is strongly indicative of particular mutations without positive confirmation results, especially considering the exponential growth in the number of new mutations and the technique optimization. There is an important diversity in early clinical features of FTDP, therefore an early in-depth DNA analysis is necessary for accurate diagnosis. Even though treatment options are limited, pedigree data and early genetic assessments are crucial for genetic counseling and possibly future clinical trials.
Disclosure: No disclosures.

EPO-220

Influence of flavonoids on the short-term memory of stressed white rats

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Background and aims: The negative impact of the stress induced by modern Megapolis noise on various forms of human memory and search for therapeutic-prophylactics means required for post-stress rehabilitation is one of the main fields of active study of neurophysiologists.
Methods: For this purpose, we used adult, intact white laboratory rats of the Krushinsky-Molodkinas line as a model object, which were divided into fear and curiosity groups according to their motivational-emotional field and individual-typological properties through the "open field" test provided by the Hull. We studied the impact of stress induced by the short, loud sound (stress factor) on short term memory and effect of total fraction of flavonoids released from (Satureja hortensis L.) on the post-stress, impaired memory rehabilitation process. The short term memory duration was determined by Acad. Beritashvili indirect method of classical spatial delayed reaction in T-like labyrinth.
Results: Experiments have shown that stress induced by loud sound dramatically worsens short-term memory in both fear and curiosity rat groups.
Conclusion: Intraperitoneal administration of a total fraction of flavonoids derived from (Satureja hortensis L.) in post-stress animals of both groups significantly improved the short-term memory rehabilitation process compared with the control group.
Disclosure: Nothing to disclose.

EPO-221

Assessment of verbal thinking in patients with diabetic encephalopathy

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Background and aims: Diabetes mellitus is one of the ten most common causes of death. One of its frequent complications is diabetic encephalopathy characterized by brain damage caused by episodes of hypoglycemia or prolonged hyperglycemia and manifested by cognitive decline (CD).
Methods: Several neuropsychological tests are used for the assessment of cognitive status in patients with diabetes mellitus (Montreal Cognitive Assessment (MoCA), Mini-Mental State Examination (MMSE), etc.). In clinical practice there is an urge to develop more sensitive scales. Speech deficit in patients with DE is detected at a late stage because standard instruments include too few tests assessing speech. The aim of the study was to develop linguistically valid diagnostic subtests revealing decline in verbal thinking.
Results: A Russian-language test (PS-test) assessing the level of understanding the units with figurative meaning was created as a result of research. It was linguistically validated in 300 informants without neurological diseases and tested in 58 patients with CD revealed by the MoCA. PS-test results correlate with the MoCA results; it is able to register speech problems when the standard screening does not reveal them.
Conclusion: Paremiological units are the subtlest diagnostic markers of CD onset. The decrease in operational thinking, ability to distract and generalize, to understand the figurative meaning are revealed at the early stages of CD. The inclusion of PS-test into the assessment of CF helps to start the treatment in time.
Disclosure: The reported study was funded by Russian Foundation for Basic Research (RFBR) according to the research project 20-312-90044.

EPO-222

Cognition and Behavior in Patients Treated for Obstructive Sleep Apnea with Continuous Positive Airway Pressure

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Background and aims: Obstructive sleep apnea (OSA) is characterized by repeated episodes of partial or complete disrupted breathing during sleep. Neurological dysfunction, such as memory loss, decreased attention and emotional regulation impairment are often related to OSA. Continuous positive airway pressure (CPAP) is described as a potential treatment to reverse those cognitive deficits. This systematic review aims to evaluate the effect of CPAP therapy on OSA-related neuropsychiatric and neurocognitive disorders.
Methods: Articles published between 2011 and 2020 were searched through PubMed, Web of Science, and Scopus. The following formula was used: "((“continuous positive airway pressure”) AND (“cognitive”)) AND (“obstructive sleep apnea”)". The inclusion criteria were observational studies with patients with OSA, without previous neurological conditions, treated with CPAP, who underwent one or more of three predetermined neuropsychological tests.
Results: Of 178 articles identified, 39 were selected for full-text reading, of which 11 studies were included in this review. A total of 612 patients were analysed before and after CPAP. A number of 353 patients underwent Montreal Cognitive Assessment’s test, which improved 2.26+2.32 points on average. Trail-Making-B attention’s test, applied in three studies (n=155), exhibited a medium increase of 5.56+3.6 points. Four studies evaluated the Beck Depression Inventory (n=208), presenting a significant decrease (3.42+1.31 points) after treatment.
Conclusion: This review suggests that CPAP treatment increases the reversibility of OSA-induced cognitive dysfunctions. However, an accurate interpretation of the results is hampered by the discrepancies between sample sizes. Further multicentric and large sample studies are needed to analyse the permanence of cognitive improvement in a long-term perspective.
Disclosure: Nothing to disclose.

EPO-223

Validation of the Armenian version of the Mini-Mental State Examination (MMSE-Arm) questionnaire

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Background and aims: Dementia is a group of neurocognitive disorders leading to impaired daily functioning of patients. The Mini-Mental State Examination (MMSE) is an originally English-language questionnaire accessible in many other languages, and a widely used clinical tool assessing cognitive impairment (CI). We aimed to validate MMSE-Arm for assessment of CI in Armenian-speaking population.
Methods: MMSE is an 11-item questionnaire with a maximum total score of 30, performed during clinical interview with the patient. MMSE represents seven domains – orientation in time and place, memory registration and recall, attention and calculation, language, and visuospatial construction. According to existing recommendations for translation of such instruments, MMSE underwent forward translation into Armenian and was back-translated by two independent groups of translators. MMSE-Arm was administered to patients diagnosed with dementia (dementia group - DG), and to control group (CG) without CI. MMSE-Arm was validated against the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V). MMSE-Arm Cronbach's alpha was 0.81. Strong correlation was obtained for test-retest results. MMSE means were compared using Mann-Whitney U test.
Results: Overall, 129 participants (mean age-64.4±11.9; F/M–55.8%/43.4%) were enrolled: 74 participants in DG (mean age-66.6±12.4; F/M=52.7%/47.3%), and 55 in CG (mean age-61.6±10.6; F/M=60.7%/39.3%). Mean values of MMSE-Arm between groups differed significantly: DG – 19.9±6.4, CG – 27.6±2.2 ($p<0.01$). As expected, MMSE-Arm adequately expressed the level of CI in DG vs CG.
Conclusion: Successful linguistic validation of the Armenian version of MMSE was performed. MMSE-Arm is a reliable tool with high internal consistency, and may be implemented in assessment of CI in Armenian-speaking population.
Disclosure: Nothing to disclose.

EPO-224

Enlarged Perivascular Spaces

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Background and aims: Perivascular spaces (PVSs) are common intersticial-filled structures, mostly innocent. When substantially enlarged, they appear in the magnetic ressonance as isointense cistic lesions. However, hydrocephalus due to mass effect can occur, especially if located at the mesencephalon.
Methods: A 54-year-old woman was hospitalized due to cognitive decline, gait instability and urinary incontinence that progressed over a year. Physical neurological examination showed psychomotor slowing, muscular strenght of the superior limbs grade four and inferior right/left limb grade 4/3; deep tendon reflexes increased at the left and left Babinski sign. Minimental state examination punctuated 10/30. Brain MRI revealed enlarged PVS at the mesencephalon and right diencephalon. There was upstream hydrocephalus and it was not possible to document flux at the cerebral aqueduct with dinamic studies of the cerebrospinal fluid (CSF), being those aspects congruent with non communicating hydrocephalus.
Results: The patient was submitted to an endoscopic ventriculostomy of the 3rd ventricle, with positive outcome after surgery. There was improvement of the cognitive performance, with minimental state examination score of 27/30, as well as considerable improvement of muscular strength.
Conclusion: In this patient, because of the chronic and progressive installation of the hydrocephalus, the clinical presentation was similar to a case of normal pressure hydrocephalus. The early surgery treatment of hydrocephalus seems to revert part of the symptomatology, even though long term results are not known
Disclosure: The authors deny having a conflict of interest.

COVID-19 2

EPO-225

MS patients treated with natalizumab during the COVID-19 pandemic: Safety and management

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Background and aims: MS patients treated with monoclonal antibodieshave an increased risk of infections, there are no enough data about COVID-19 infection. Natalizumab is a monoclonal antibody indicated in highly active Relapsing-Remitting MS. We aim to study the safety and management of MS patients on natalizumab during the COVID-19 pandemic.

Methods: Prospective study of MS patients on natalizumab during COVID-19 pandemic considering risk of COVID-19 infection coming to day hospital for the infusion, disease risk and risk of delaying/stopping treatment. We evaluate demographic features, time on natalizumab and dose interval and COVID-19symptoms. RT-PCR COVID-19 tests from nasopharyngeal sample was performed before natalizumab treatment.

Results: We analyzed 68 patients treated with natalizumab, 70% women and a mean age of 43 years, treated with natalizumab for 67 months (range: 2–139). In 33% of patients natalizumab treatment was changed from every four weeks to every six weeks to decrease visits to the hospital, 41% of patients continued receiving natalizumab every four weeks During first wave (March–June 2020), five patients suffered from COVID-19, four showed mild symptoms and one multilobar pneumonia solved with treatment. From May 2020 to January 2021, 451 nasal swab PCR COVID-test were carried out 24–72 hours before natalizumab infusion. 12 patients showed a positive result and natalizumab was stopped; test was repeated 1–2 weeks later with a negative result and natalizumab was restarted. Overall, 17 patients had COVID-19, nine asymptomatic and only one required hospitalization (tables 1–2).

Sex	Age	Natalizumab dosage	Time on natalizumab	Symptoms	PCR	Time
Woman	44	6w	12 m	Yes	Positive	First wave
Woman	30	6w	44 m	Yes	Positive	First wave
Man	36	6w	12 m	Yes	Not performed	First wave
Man	34	4w	130 m	Yes	Not performed	First wave
Woman	35	4w	79 m	Yes	Not performed	First wave
Woman	43	6w	79 m	No	Positive	Second wave
Man	52	6w	139 m	No	Positive	Second wave
Woman	46	6w	131 m	No	Positive	Second wave
Woman	49	4w	32 m	No	Positive	Second wave
Woman	21	6w	48 m	No	Positive	Second wave
Woman	31	4w	67 m	No	Positive	Second wave
Woman	21	6w	38 m	No	Positive	Second wave
Woman	35	6w	58 m	No	Positive	Second wave
Woman	31	6w	64 m	Yes	Positive	Second wave
Woman	32	6w	44 m	Yes	Positive	Second wave
Man	35	6w	19 m	No	Positive	Second wave
Man	48	4w	72 m	Yes	Positive	Second wave

Table 1. Characteristic of patient with Covid-19 infection

Table 2. Characteristic of COVID-19 disease

Conclusion: Natalizumab treatment seems to be safe in MS patient during COVID-19 pandemic. Most patients were asymptomatic. In some cases natalizumab was delayed but not discontinued.

Disclosure: Nothing to disclose.

EPO-226

The relationship between HSV, a trivial cause of meningitis, and the "new" SARS-CoV-2 clinical cases

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Background and aims: The potential involvement of the CNS in COVID-19 attracts considerable attention due to the variety of neurological manifestations presented during or as a result of the disease process. HSV-1 most commonly causes encephalitis, and the most common neurological complication of HSV-2 infection is aseptic meningitis.
Methods: To present cases of meningitis patients with clinical and CSF findings corresponding to herpes meningitis diagnosed during or shortly after COVID-19 disease and to analyze the potential relationship between the two diseases.
Results: We present four cases of patients with clinical and laboratory data for viral meningitis diagnosed during or shortly after SARS-CoV-2 infection. The four patients were young people, without concomitant diseases. We found mild protein-cell dissociation in the CSF. CSF virology rejected the presence of SARS-CoV-2, but all four patients tested positive for CSF for herpes viruses. All four patients were treated according to a viral neuroinfection treatment protocol and had a good clinical response with complete recovery.
Conclusion: We compared our experience in terms of clinical course, performed research, treatment and the corresponding response to it, with the cases published so far. Patients were expected to have SARS-CoV-2 meningitis with a history of epidemiology. Despite the lack of evidence for SARS-CoV-2 in CSF, we hypothesize an indirect link between infection and the onset of herpes meningitis. The probable cause is that severe infection with SARS-Cov 2, similar to other severe viral infections, results in a change in the T-cell response. This process leads to increased susceptibility to other viral infections.
Disclosure: Nothing to disclose.

EPO-227

Long-lasting Cognitive impairment after COVID-19

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Background and aims: SARS-CoV-2 involves the Central Nervous System (CNS) and causes neurological symptoms. In this study, we aimed to evaluate cognitive functioning in the months following hospital discharge.
Methods: We recruited 38 (aged 22–74 years; 27 males) patients hospitalized for complications of SARS-CoV-2 infection in non-intensive COVID-19 units. Participants underwent neuropsychological testing about five months (18.98±5.17 weeks) after hospital discharge.
Results: 42.1% of patients showed processing speed deficits (Symbol-Digit Modalities Test), while 26.3% showed delayed verbal recall deficits (Serial Recall Test Delayed recall [SRT-D]). 21.0% presented with deficits in both processing speed and verbal memory. Acute respiratory distress syndrome (ARDS) during hospitalization was associated with worse verbal long-term memory performance (ARDS vs. no ARDS: SRT-D mean score= 5.95±2.56 vs. 8.10±2.62, p=0.029).
Conclusion: We found that cognitive abnormalities can be frequently observed in COVID-19 patients, even months following hospital discharge. Deficits of concentration, memory, and overall decreased cognitive speed can interfere with work and daily activities, and therefore deserve attention, especially in younger subjects.
Disclosure: The authors declare no conflict of interest.

EPO-228

Acute asymmetrical painful motor and sensory axonal neuropathy post COVID-19 infection, a case report

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Background and aims: Peripheral and central nervous systems affection as a complication of COVID-19 were reported. This could be related to the direct effects of virus on the nervous system as post-infectious immune mediated effect or neurological complication of systemic effect of COVID-19.

Methods: A previously healthy 44 years old male patient presented to our hospital after four weeks of onset of COVID-19 symptoms that included fever, pharyngitis and cough. He complained of left foot paresthesia associated with weakness of left toes, followed by weakness and numbness of right upper limb distally followed by left upper limb weakness distally then few days later numbness of right lower limb. There were no dysautonomic or sphincter abnormalities. Cranial and respiratory nerves were normal. Examination showed generalized areflexia, tenderness of calf muscle and positive straight leg raise test. MRI brain and spinal cord, nerve conduction velocity (NCV), CSF examination, full laboratory including were investigated.

Results: MRI brain and cord showed no abnormality. CSF result showed clear colorless fluid, CSF protein 54.4gm/dl, and cell count 3/mm^3. NCV, motor figure 1 and sensory figure 2, showed mixed axonal motor and sensory polyneuropathy. A high-dose intravenous human immunoglobulin (IVIG 0.4g/kg for five days) was prescribed. He has been stable for the following two weeks. At last visit, four weeks after IVIG infusion, patient reported significant clinical improvement, persisting only with mild right upper limb numbness.

Motor nerves	Latency (ms)	Amplitude (mV)	CV (m/s)	AMP %	F-M (ms)
Right median					26.4
wrist-APB	3.2	9.6			
Elbow-Wrist	7.8	9.2	36.5	-6	
Axilla-Elbow	10	8.5	39.1	-8	
Left median					26.6
wrist-APB	3.2	10	36.5	-7	
Elbow-Wrist	7.8	9.7	65	-9	
Axilla-Elbow	9	9.3			
Right ulnar					29.1
wrist-ADM	3	7.3			
B.Elbow-Wrist	7.8	7	54.2	-5	
A.Elbow-B.Elbow	9.5	6.5	58.8	-7	
Left ulnar					28.8
wrist-ADM	2.5	7.2			
B.Elbow-Wrist	7.8	6.8	52.8	-7	
A.Elbow-B.Elbow	9.4	6.6	62.5	-8	
Right tibial					50
Ankle-AH	5.2	7.6	40	-20	
Pop Fos-ankle	13.2	5.9			
Left tibial					51.4
Ankle-AH	4.6	1.3			
Pop Fos-ankle	16.4	0.8	35.6	-63	
Right Peroneal					
Ankle-EDB	5.7	0.3			
Fib Hd-ankle	14.4	0.2	39.1	-67	
Pop Fos-Fib Hd	16.3	0.2	47.4	-6	
Left Prox. Peroneal					
Fib Hd-Tib Ant	3.5	1	42.9	-34	
Pop Fos-Fib Hd	5.6	1			

Motor nerve conduction velocities

Sensory nerves	Latency (ms)	AMPlitude (uV)	CV (m/s)
Right median			
wrist-Index	3.7	7.1	58.3
Left median			
wrist-Index	3.5	5.3	51.9
Right ulnar			
wrist-5th Dig	3	28	52.4
Left ulnar			
wrist-5th Dig	3	43	52.4
Right sural			
Stim1-Rec1	3.8	6.9	53.8
Left Sural			
Stim1-Rec1	5.2	4.5	35.9

Sensory nerve conduction velocities

Conclusion: We described a case of acute asymmetrical painful polyneuritis, atypical GBS, and suggest it could be an atypical neurological manifestation related to COVID-19 infection.

Disclosure: No disclosure to declare.

EPO-229

Electrofunctional results in children with COVID-19

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Background and aims: COVID-19 infection may cause nonspecific EEG changes.
Methods: We have analyzed 48 results of EEG in children with COVID-19 (confirmed by molecular RT-PCR examinations). The EEG was performed and was described by qualified specialists.
Results: We have found the abnormal background activity on EEG (97.9% [95% CI: 95.84–99.96]; p<0.01), generalised slowing (93.8% [95% CI: 90 , 31.2–97.29]; p<0.01); epileptiform discharges (ED) (33.3% [95% CI: 40.1–26.5]; p<0.01). ED was increased in patients with seizures (62.5% [95% CI: 74.6–50.4]; p=0.52) and a history of epilepsy (43.8% []. 95% CI: 56.2–31.4]; p=0.47), comparing to those without such manifestations (37.5% [95% CI: 49.6–25.3]; p=0,05). Among children with ED, persisted seizures more than 1–2 weeks were found (31.3% [95% CI: 42.89–19.71]; p=0.054), in others – more than one month (12.5% [95%: 20.77–4.23]; p=0.075). Some children developed epilepsy (18.8% [95% CI: 28.56–9.04]; p=0.08), two of them have showed drug resistance.
Conclusion: COVID-19 can cause EEG changes, the most common being expressed by abnormal background activity (97.9%) and generalized slowdown of EEG route (93.8%). Epileptic discharges are less common (33.3%), with an increased proportion in children with seizures (62.5%) and a history of epilepsy (43.7%). COVID-19 can also cause remote epilepsy.
Disclosure: Nothing to disclose.

EPO-230

A retrospective single-center clinical study of the patients with COVID-19 in the Republic of Dagestan, Russia

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Background and aims: COVID-19 is a rapidly emerging respiratory disease caused by SARS-CoV-2. Numerous studies have demonstrated that patients with COVID-19 may develop neurological complications. Despite this, the available data on the clinical characteristics of affected patients remain limited. The purpose of the study was to present the clinical manifestations and predictors of severe outcome of COVID-19 patients examined outpatiently at the Diagnostic Center of the Republic of Dagestan, Russia.
Methods: A retrospective single-center study of the 175 patients with confirmed COVID-19 was conducted from 1st May 2020 to 30th June 2020. Epidemiological, demographic, clinical, laboratory and radiological data were collected and analyzed. All patients were divided into four groups based on their chest CT scans: CT-0 – no evidence of pneumonia, CT-1 <25% involvement, CT-2 – 25 to 50%, CT-3 – 50 to 75%, CT-4 > 75% involvement.
Results: 175 COVID-19 patients were enrolled during the study period. The mean age was 49.8±12.3 years. Female was the dominant sex (64%). The leading neurological signs were fatigue (81.2%), headache (64.6%), anosmia/ageusia (54.8%/52.0%), anxiety/depression (58.8%/57.7%). A comparative analysis revealed no significant differences in the prevalence of neurological symptoms in patients with different severity of lung involvement. Older age, female sex and comorbidity – obesity, arterial hypertension and diabetes mellitus were estimated as higher risk factors for severe form.
Conclusion: The first Russian retrospective study of COVID-19 adult patients was presented. There were no patients in our cohort with a new-onset neurologic event. The main neurological manifestations were comparable in frequency to those reported in the literature.
Disclosure: Nothing to disclose.

EPO-231

Teleneurology during the COVID-19 pandemic: experiences and challenges

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Background and aims: This survey aimed at providing a comprehensive assessment of the rapid implementation of Teleneurology services at University Hospitals of Leicester in England in response to the COVID-19 pandemic. The twin surveys explored the experiences of both patients and clinicians.

Methods: A target of 10% of patients who had audio consultations in the department of neurology was set for the patients' survey. The total number of patients was 1100 during the month of May. A simple randomised procedure was followed for patient' selection; every 10th patient in the list was contacted by phone by the auditors.

Results: 44% of patients rated their experience as similar to their face-to-face appointments; whilst 18% rated their experience as better. 42% (19/45) of patients would prefer a face-to-face appointment over a phone appointment as opposed to 38% (17/45) who prefer audio consultation. Clinicians identified subspecialties such as movement disorders, neuromuscular and dementia clinics as particularly challenging to conduct over the phone as opposed to headache and epilepsy clinics. When asked to rate their experience of audio clinics, no clear preference was expressed.

Conclusion: Data from these twin surveys suggests teleneurology under the unique circumstances imposed by the COVID-19 pandemic has cautious positive reception from patients and a careful welcome from clinicians. Teleneurology is feasible and effective method for service delivery in appropriately selected patients. Careful patient selection, implementation of validated protocols and introduction of bi-directional videoconferencing would help address some of the shortcomings and enhance the experience of both patients and clinicians.

Disclosure: Nothing to disclose.

EPO-232

Clinical presentations of Guillain-Barré syndrome exacerbated by COVID-19

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Background and aims: Guillain-Barré Syndrome (GBS) is a syndrome of acute immune-mediated polyneuropathies. It is usually preceded by an infection, the most common of which are campylobacter, cytomegalovirus, Epstein-Barr virus, and, more recently, Zika virus and COVID-19. Since the beginning of the pandemic caused by the COVID-19, rare cases of GBS related to the virus have been described. This work reviews the clinical presentations.

Methods: A systematic review was made according to the PRISMA protocol, on MEDLINE and LILACS, following this applied formula: ("guillain barre" [Title / Abstract]) AND ("covid" [Title / Abstract]). We included control cases and series of cases, written in English, Portuguese and Spanish, describing the GBS of patients regarding temporality, evolution, and affected limbs.

Results: Of the 192 articles found, 61 were selected for a full reading. These, 10 were incorporated into the scope of this study. As for temporality, the presentation of GBS triggered by COVID-19 is similar to other infections, with the onset of weakness symptoms after five to 10 days; in terms of characteristics, COVID-19 causes an acute inflammatory demyelinating polyradiculoneuropathy GBS, with the usual reports of acute sensorimotor axonal neuropathy, and rare cases describing other subtypes, with no difference in the frequency of GBS according to the severity of COVID-19.

Conclusion: The current literature demonstrates the association between COVID-19 and GBS. This review demonstrates a standardization of the clinical condition of these patients, in a way that raises the need for further studies to improve management

Disclosure: The authors declare that they have no competing interests.

EPO-233

Cerebral vasoregulation dysfunction after SARS-Cov-2 infection

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Background and aims: SARS-Cov-2 disease could cause endothelial dysfunction, damage to the blood brain barrier and microvascular alteration, thus having the ability to cause different pathologies. Because these alterations can be subtle, they can be unnoticed except in susceptible individuals.
Methods: We present the case of a 25-year-old male with history of Chiari type II malformation, severe triventricular hydrocephalus, ventriculoperitoneal bypass carrier with programmable valve and chronic kidney disease because of which, he has been on dialysis for several years. In April 2020, he developed severe pneumonia from SARS-CoV-2 infection, receiving treatment with Tocilizumab. After that, it presented several episodes during the initial phase of dialysis of decreased level of consciousness, arreactive pupils an minute-long decerebrate posture, without other associated clinic.
Results: The EEG performed during the episodes showed no epileptic discharges and neuroimaging performed after the dialysis, showed no change from previous ones. Transcranial doppler was performed during the episodes, observing a high arterial pulsatility index which may reflect an increase in peripheral resistances, likely related to intracranial hypertension during the initial phase of dialysis that would cause the clinic. The patient was referred to neurosurgery for decrease of valvular pressure, with clinical resolution.
Conclusion: The increase in intracranial pressure that occurs during the initial stages of dialysis, along with the baseline characteristics of the patient may be related to the clinic presented by this patient. This could lead to an alteration of secondary cerebral vasoregulation to possible endothelial dysfunction caused by the new coronavirus, which in other patients could go unnoticed.
Disclosure: Nothing to disclose.

EPO-234

Neurological manifestations and outcomes in Sudanese patients diagnosed with COVID-19 in Khartoum state, Sudan

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Background and aims: COVID-19 is considered a newly emerged disease which is affecting multiple systems inside the human body including nervous systems by causing different neurological symptoms. There are fewer studies about neurological manifestations which is caused by COVID-19. For that, we aimed to study these neurological manifestations Sudanese patients with COVID-19.
Methods: A retrospective hospital based study design was implemented using hospital records at selected hospitals at Khartoum state. We included all patients with COVID-19 who are suffering from unusual neurological manifestations. Demographics data, comorbidities, clinical investigations and outcomes of patients with neurological manifestations were collected and analyzed using SPSS.
Results: A total of 31 patients with a mean age 65±16 were included. 21 (67.5%) of them were male with median (IQR) oxygen saturation 94 (83–98). The most common comorbidities were hypertension 17 (68%) and diabetes nine (36%). Regarding neurological symptoms, most of them present with disturbed level of consciousness 26 (84%)and hemiparesis seven (Table 1). Regarding outcomes, the overall mortality for 23 documented patients was 11 (48%) with a longer median hospital stay for discharged patients 6.0 (3.5 –10.0) days, and the most common complication were acute respiratory distress syndrome three (19%) and respiratory failure four (25%). Other laboratory investigations were shown in Table 2.

Characteristic	N	N = 31[1]
Age, years	30	65 (60, 76)
Gender:	31	
Female		10 (32.5%)
Male		21 (67.5%)
Severity of the disease at the time of admission	14	
Critically ill		10 (71.1%)
Moderate		1 (7.1%)
Severe		3 (21%)
Length of stay, days	21	6.0 (2.0, 9.0)
In hospital disposition since admission to hospital:	24	
HDU Disposition		4 (17%)
ICU Disposition		10 (42%)
Ward Disposition		10 (42.2%)
Vital Sign:		
Heart rate (Beat per minutes)	21	95 (79, 110)
Systolic Blood pressure (mm HG)	23	130 (104, 140)
Diastolic blood pressure (mm HG)	23	77 (68, 88)
Respiratory rate (breath per minutes)	14	30 (20, 42)
$SaPO^2$, percentage	19	94 (83, 98)
Comorbidities:		
Diabetes mellitus	25	9 (36%)
Hypertension	25	17 (68%)
Asthma	25	2 (8.0%)
Pulmonary Tuberculosis	25	0 (0%)
Cardiovascular diseases (IHD, heart failure, arrhythmia)	25	5 (20%)
Chronic renal diseases	25	5 (20%)
Chronic liver diseases	25	0 (0%)
Cerebrovascular diseases	25	4 (16%)
Smoking	25	1 (4.0%)
Drinking alcohol	25	0 (0%)
General presentations:		
Fever	19	17 (89%)
Headache	19	1 (5.3%)
Fatigue	19	11 (58%)
Loss of smell sensation	19	0 (0%)
Loss of taste	19	0 (0%)
Muscles or body aches	19	0 (0%)
Neurological symptoms		
Disturbed level of consciousness	31	26 (84%)
Hemiparesis	31	7 (23%)
Hemisensory deficits	31	3 (9.7%)
Aphasia	31	3 (9.7%)
Visual loss	31	1 (3.2%)
Respiratory symptoms:		
Cough	20	13 (65%)
Shortness of breath	20	16 (80%)
Congestion or runny nose	20	0 (0%)
Chest pain	20	0 (0%)
Hemoptysis	20	1 (5.0%)
Gastrointestinal symptoms:		
Nausea or vomiting	7	5 (71%)
Diarrhea	7	3 (43%)
Abdominal pain	7	1 (14%)
Loss of appetite	7	1 (14%)

[1] Statistics presented: Median (IQR); n (%)

Table 1 : baseline characteristic for COVID-19 patients present with neurological symptoms.

Characteristic	N	Overall, N = 23[1]	Death, N = 11[1]	Discharged home, N = 12[1]	p-value[2]
Laboratory investigations:					
White blood cells, x103/µL	17	13.4 (9.1, 14.6)	13.6 (9.4, 14.5)	10.9 (8.0, 14.7)	0.9
Monocyte , x 103/µL	10	0.60 (0.43, 0.75)	0.55 (0.30, 0.78)	0.62 (0.51, 0.74)	0.8
Lymphocyte, x103/µL	14	1.03 (0.52, 1.70)	0.95 (0.55, 1.80)	1.08 (0.56, 1.40)	>0.9
Neutrophils , x103/µL	12	11.6 (9.4, 13.4)	12.3 (11.5, 14.2)	9.1 (5.3, 12.0)	0.13
Red Blood Cells , million/mm3	10	4 (3, 5)	4 (3, 5)	4 (4, 36)	>0.9
Hemoglobin, g/dL	15	9.30 (7.85, 11.20)	9.30 (7.80, 10.90)	9.75 (8.05, 11.30)	0.9
Platelets , x109/L	16	202 (132, 307)	186 (105, 267)	219 (146, 430)	0.4
C-Reactive Protien , mg/dl	13	122 (106, 164)	131 (114, 157)	108 (43, 164)	0.7
Renal function test and electrolytes:					
Random blood sugar , mg/dL	11	145 (118, 182)	182 (130, 254)	124 (120, 136)	0.3
Sodium , mmol/L	17	137 (128, 148)	137 (132, 140)	140 (123, 150)	>0.9
Potassium , mmol/L	17	3.90 (3.00, 5.20)	4.00 (3.00, 5.20)	3.75 (3.08, 4.82)	0.7
Blood Urea nitrogen, mg/dL	14	72 (46, 108)	72 (49, 110)	72 (45, 101)	0.8
Serum Creatinine , mg/dL	16	1.67 (0.92, 2.28)	1.80 (0.70, 2.20)	1.64 (1.35, 3.30)	0.8
Liver function test:					
Alanine aminotransferase , U/L	10	60 (31, 112)	84 (36, 148)	36 (32, 55)	0.5
Aspartate aminotransferase , U/L	10	74 (42, 102)	80 (54, 98)	45 (40, 82)	0.8
Alkaline phosphatase , U/L	11	146 (84, 209)	146 (94, 170)	166 (80, 591)	0.6
Albumin , g/dl	11	2.80 (1.90, 3.20)	2.15 (1.75, 2.90)	3.20 (3.10, 3.25)	0.2
Short term outcome within 15 days :	20				<0.001
Death		11 (55%)	11 (100%)	0 (0%)	
Discharge home		6 (30%)	0 (0%)	6 (67%)	
Transferred to ICU		3 (15%)	0 (0%)	3 (33%)	
Length of stay, days	20	5.5 (2.0, 8.2)	3.0 (1.0, 8.0)	6.0 (3.5, 10.0)	0.3
Does patient required any respiratory support?	15	5 (33%)	4 (57%)	1 (12%)	0.12
In hospital complication:	16				
Acute respiratory distress syndrome	16	3 (19%)	2 (18%)	1 (20%)	>0.9
Respiratory failure	16	4 (25%)	4 (36%)	0 (0%)	0.2
Acute cardiac injury	16	1 (6.2%)	1 (9.1%)	0 (0%)	>0.9
Heart failure	16	2 (12%)	2 (18%)	0 (0%)	>0.9
Sepsis	16	5 (31%)	3 (27%)	2 (40%)	>0.9
Acidosis	16	6 (38%)	6 (55%)	0 (0%)	0.093
Alkalosis	16	2 (12%)	1 (9.1%)	1 (20%)	>0.9
Acute kidney injury	16	4 (25%)	3 (27%)	1 (20%)	>0.9
Disseminated Intravascular Coagulopathy	16	0 (0%)	0 (0%)	0 (0%)	
Hyperkalemia	16	2 (12%)	2 (18%)	0 (0%)	>0.9
Hypokalemia	16	3 (19%)	0 (0%)	3 (60%)	0.018
Hypernatremia	16	1 (6.2%)	0 (0%)	1 (20%)	0.3
Hyponatremia	16	2 (12%)	1 (9.1%)	1 (20%)	>0.9
Shock	16	2 (12%)	2 (18%)	0 (0%)	>0.9
Acute liver injury	16	0 (0%)	0 (0%)	0 (0%)	
Gastrointestinal bleeding	16	1 (6.2%)	1 (9.1%)	0 (0%)	>0.9

[1] Statistics presented: Median (IQR); n (%)

[2] Statistical tests performed: Wilcoxon rank-sum test; Fisher's exact test

Table 2: Laboratory profile and outcomes for COVID-19 patients with neurological symptoms.

Conclusion: Patients with COVID-19 are presented in a critically ill status and they have a higher in hospital mortality rate. Special management and care is needed to decrease the mortality and improve outcome among these COVID-19 patients with neurological symptoms.

Disclosure: Nothing to disclose.

EPO-235

SARS-CoV-2 and cerebrovascular disease: Casual or Causal Role?

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Background and aims: Coronavirus SARS-CoV-2 is currently the major public health concern worldwide with systemic complications, including thrombotic and hemorrhagic neurological manifestations.
Methods: We report a series of patients admitted in the stroke unit of neurology department of the Military Hospital of Tunis in November 2020, presented with cerebrovascular symptoms as an initial presentation of SARS-CoV-2. Clinical characteristics and outcome of the patients are described.
Results: Seven patients were included. Infection with SARS-CoV-2 was diagnosed through reverse transcription polymerase chain reaction (RT-PCR) of tracheal aspirate and a chest computed tomography (CT) scan. The main cerebrovascular manifestations are: acute ischemic stroke (AIS) in five patients, intracerebral hemorrhage in one case, with a left capsulo thalamic localization. One patient presented with cerebral venous thrombosis (CVT) in the left sigmoid sinus. All patients with AIS received antiplatelet therapy and statins. Treatment of COVID-19 infection with antibiotics, vitamins and preventive anticoagulant has been initiated. three patients developed dyspnea and oxygen desaturation with need of Oxygen support by face mask. One patient was transferred to the intensive care unit and required intubation, and one patient died after two days. The patient with CVT was started on full anticoagulation with unfractionated heparin relayed by oral anticoagulants. After one week, she was stabilized.
Conclusion: SARS-CoV-2 is a major risk factor for cerebrovascular disease. Better understanding of these complications is urgent in order to improve the management of these patients.
Disclosure: Nothing to disclose.

EPO-236

The emotional impact of social distancing in general Romanian population during COVID-19 pandemic

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Background and aims: The recent onset of pandemic with COVID-19 and the social distancing measures had important consequences all over the world, including on the emotional level. The aim of this study was to assess the emotional impact of social distancing in general Romanian population during COVID-19 pandemic.
Methods: An online questionnaire was distributed on social networks. The questionnaire comprises 94 questions covering various fields, including socio-demographic data, the overall emotional impact, level of distress and feelings during lockdown.
Results: The sample consists of 350 people, of whom 70.6% (n=247) are women. The age of the participants was between 18–74 years. The respondents were asked about the emotional impact of the social distancing measures. We evaluated psychological symptoms such as depression, anxiety, insecurity. The samples' feelings were distributed evenly, as we noticed that one third of the population had low levels of depression, anxiety, fear, agitation, insecurity, confusion. one third of the respondents had also moderate levels and the same percentage of the respondents had high levels of these feelings. Few people felt the same as they did before the pandemic (23.7%), they noticed a change in their appetite (44.6%), but they didn't have trouble sleeping (41.4%) and didn't feel alone (47.4%). Most of them took the chance to spend more time with their loved ones and to develop new hobbies.
Conclusion: Social distancing is causing emotional distress at high level in the general population during COVID-19 pandemic.
Disclosure: Nothing to disclose.

EPO-237

The emotional impact of social distancing during the COVID-19 pandemic in Romanian patients with Parkinson's disease

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Background and aims: The COVID-19 pandemic has been declared an international public health emergency, considering the various severe consequences on human health. Several restrictive measures (e.g. forced quarantine) were adopted worldwide, including Romania, in order to slow down the transmission of the virus. The aim of this study was to assess the emotional impact of social distancing in Romanian PD patients during COVID-19 pandemic, first wave.
Methods: We used an online questionnaire that was distributed on social networks. The questionnaire included questions covering: socio-demographic data, overall impact, level of suffering and feelings of patients with Parkinson's disease (PD). There were 102 respondents.
Results: The results of this study suggest that the COVID-19 pandemic also has a significant emotional impact on people with PD, especially in older people. This is observed in the higher frequency of certain feelings (fear – 70%, frustration – 65%, helplessness – 50%) in people over 50 years of age compared to those under this age (40%, 20%, 20% – for the same feelings). In addition, during this period 44.1% of respondents felt more depressed, 68.6% had sleep problems, 43% experienced a deterioration in health and only 27.5% of participants said that the pandemic did not affect their lives. Regarding the opinion on the social distance measures imposed, 91% of the respondents consider them necessary and 9% consider them exaggerated.
Conclusion: The emotional impact of social distancing of PD patients during the COVID-19 pandemic was high. There is need for more strategies to better cope with the negative consequences for mental health.
Disclosure: Nothing to disclose.

EPO-238

MRI-negative acute transverse myelitis during COVID-19 pandemic: A case report

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Background and aims: Magnetic reasoning imaging (MRI) negative acute transverse myelitis (ATM) coincided with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has rarely been reported so far.
Methods: We report a 39-year-old male with recent onset of symptoms indicative, though not established with reverse transcriptase polymerase chain reaction (RT-PCR), coronavirus disease 19 (COVID-19), namely fever, cough, fatigue, myalgias, anosmia and hypogeusia. Eight days later he gradually exhibited lower body hypesthesia/paresthesia, Lhermitte sign, gait disturbances and bladder dysfunction. The patient was deteriorating for the next 15 days. He was admitted soon thereafter, and a complete clinical and laboratory investigation was performed.
Results: High titers of serum anti-SARS-CoV-2 IgG antibodies confirmed COVID-19, while RT-PCR resulted negative. Neurological examination revealed a T11 segmental sensory level and sensory ataxia and pyramidal tract involvement of lower extremities. Brain and spine MRI were normal. Abnormal somatosensory evoked potentials confirmed large-fiber sensory system functional deficit. Cerebrospinal fluid analysis showed lymphopleocytosis and type four oligoclonal bands, while RT-PCR and anti-SARS-CoV-2 antibodies were negative. Thorough investigation excluded other possible causes of MRI-negative ATM and revealed an IgG-lamda monoclonal gammopathy of undetermined significance in the absence of malignancy evidence. The patient partially improved after treatment with intravenous methylprednisolone.
Conclusion: We presented a case of MRI-negative ATM possibly, though not proven to be, attributed to a COVID-19-associated immune-mediated inflammatory response. In our case there was a close temporal correlation between COVID-19 symptoms onset and ATM development. To our knowledge this is the first reported case from Greece and the second one worldwide of COVID-19-associated MRI-negative ATM.
Disclosure: Nothing to disclose.

Critical care

EPO-239

Ruptured blood blister-like aneurysm of rare location successfully treated by flow-diversion device: case report

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Background and aims: Blood blister-like aneurysms (BLAs) are a rare pathology of intracranial arteries accounting for less than 1% of all aneurysms. They commonly arise from internal carotid artery (>90%), while locations such as the the basilar artery are considered atypical. Furthermore, according to results of histological examination of blister aneurysms their pathogenesis might be the same as of pseudoaneurysm but without clear evidence of dissection.
Methods: Case report and literature review.
Results: We report a case of a basilar artery BLA successfully treated with Pipeline Embolization Device in the setting of acute subarachnoid hemorrhage (SAH). The patient presented with severe headache and subsequently developed neurological deficits, ultimately requiring intubation and full intensive care. After endovascular treatment he gradually recovered, remaining severely disabled (mRS 4). Eight months after the initial SAH repeated angiography showed complete obliteration of the aneurysm but his clinical state remained the same.
Conclusion: Current data on BLA pathophysiology, diagnostics and treatment is scarce, especially for atypical locations. Treatment of basilar artery BLA with Pipeline Embolization Device is an effective endovascular option alongside neurosurgical management.
Disclosure: Nothing to disclose.

EPO-240

Delirium at patients in acute stage of Stroke

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Background and aims: Delirium is a syndrome that can develop on the background of many diseases.
Methods: We conducted an observational study of 40 patients admitted to the intensive care unit for patients with acute neurologic pathology. Patients were divided into two groups – the first group (n=17, 42.5%) patients with delirium and the second group (n=23, 57.5%) – patients without delirium. We studied types of stroke in the study groups. The presence of delirium was carried out on the scale ICDSC in the first 24–48 hours from the moment of admission; also, we assessed patients from the CGS, FOUR and RASS scale. Statistical analysis was performed using the Mann-Whitney test and Pearson's chi-squared test, the changes were considered statistically significant at p=0.05.

	Sex, m/f	Age, year M±σ	p
1 group	7 (41%)/10 (59%)	60.2±11.0	>0.05
2 group	14 (61%)/9 (39%)	64.1±15.1	>0.05

Characteristics of patients (Table. 1)

Results: In the first group, ischemic stroke (IS) was diagnosed – 11 (65%) patients, hemorrhagic stroke (HS) – six patients (35%), of them in the form of intracerebral hematoma (ICH) – three patients (17.5 %) and in the form of subarachnoid hemorrhage (SAH) – three patients (17.5%). In the second group, IS was diagnosed in 16 patients (70%), HS – in seven patients (30%), ICH – six patients (25.6%) and SAH – one patient (4, 4%). In the first group subsyndromal delirium was diagnosed in 12 patients (71%), delirium was diagnosed in five patients (29%). From five patients with delirium two patients had hypoactive delirium, one patient – hyperactive, two patients –mixed delirium.

	CGS	FOUR	RASS
1 group	14 [9;15]	16 [9;16]	0 [-3;0]
2 group	15 [14;15]	16 [16;16]	-1 [-1;0]
p	<0.05	<0.05	<0.05

The depression of consciousness, the presence of sedation/agitation, Me [25;75](Table 2.)

Conclusion: The frequency of delirium in patients with Stroke was 42.5%.
Disclosure: We had no relevant disclosures.

EPO-241

Utility of Short-term EEG Monitoring in the Pediatric Intensive Care Unit

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Background and aims: The study aims to explore the underlying etiologies and outcome in children who underwent EEG monitoring at pediatric intensive care unit (PICU).
Methods: Critically ill children who underwent EEG monitoring (0.5–1 hours) in the PICU at Hacettepe University Children's Hospital between January 2019 and June 2019 were retrospectively studied. Functional outcome was assessed with the modified Rankin Scale (mRS) at latest follow up visit.
Results: 35 patients aged 2.2–12 years, median 4.5 years, 24 (68.5%) of them male, were included. The most common underlying condition was encephalitis (10/35, 28.6%) followed by hypoxic/hypercapnic respiratory failure, acute traumatic brain injury, systemic infection/disease, and others. six patients (17.1%) had preexisting neurological disorders including epilepsy (n=2). Indications for EEG monitoring were altered mental status (n=17), seizures (n=11), and abnormal movements or fluctuations in vital signs (n=7). Normal background activity was observed in six patients, one patient had burst-suppression pattern; in the remaining cases EEG background was slow/disorganized (n=12), low-suppressed voltage was noted in 16 patients. Four patients (11.4%) had epileptiform discharges, three (8.5%) had electrographic seizures without clinical signs. The PICU length of stay was 24 (3–60) days; 15 patients (42.8%) had excellent outcome (mRS 0-1).
Conclusion: Our results suggest that short term EEG monitoring may detect electrographic seizures and background changes, and may help to guide management of critically ill children with diverse etiologies when continuous EEG is not available.
Disclosure: Nothing to disclose.

EPO-242

Metabolomic profiles of patients with unresponsive wakefullness syndrome

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Background and aims: Over the past decades, metabolomics has grown exponentially and so has the number of articles related to metabolomics.
Methods: Ultra-high-performance liquid chromatography and quadrupole time-of-flight mass spectrometry (ultra-highperformance liquid chromatography coupled with quadrupole time-of-flight mass spectrometry (UHPLC-Q-TOF-MS)) were used to evaluate blood plasma metabolomic profiles. At the first stage, a comparison was made between pooled samples from unresponsive wakefulness state (UWS) patients (n=8) . Venous blood was taken from the jugular vein, with the insertion of the end of the catheter retrograde and arterial blood was taken. Samples were collected twice a day and night with one hour difference, 2 days in a row. To assess the differences between the groups, the MS-DIAL review metabolomics software was used (http://prime.psc.riken.jp/compms/msdial/main.html).
Results: As a result of UHPLC-Q-TOF-MS analysis and after subtracting the signals present in the shame sample, 2,528 potential metabolites were identified. The number of signals correlated by exact mass with metabolites in the database was 949. When comparing groups with a one-hour fence difference, no statistical differences was found. For the day/night groups, 46 signals with the most significant difference were selected. For accurate confirmation, use of standart substance is planned.
Conclusion: Understanding biological mechanisms in UWS patients at the molecular level (biological components) , the effects of an ongoing biological process in the organism as a whole (biological functionality) is very important for prognosis and treatment approach
Disclosure: The study is supported by the grant of the RFFR 19-29-01066.

EPO-243

Pupillometry and invasive monitoring in neurointensive care unit

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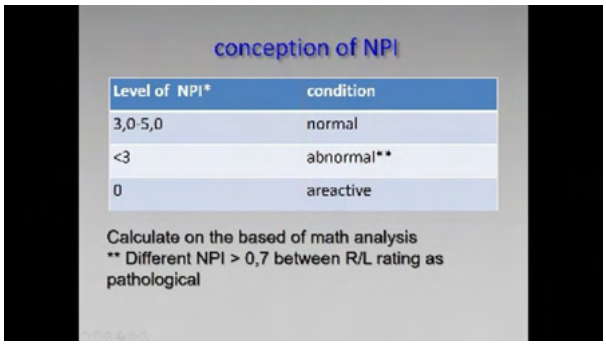
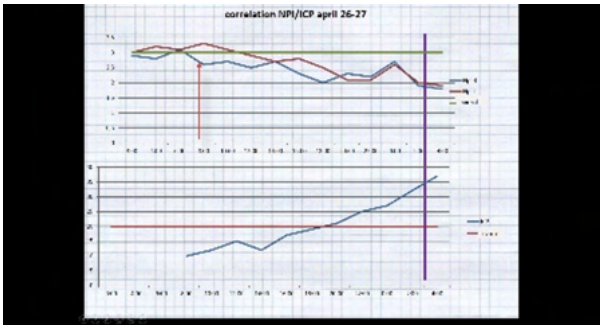
Background and aims: An invasive measurement of intracranial pressure is the most informative component of neuromonitoring, but requires surgical intervention. In recent search for predictors of ICP increase to clarify the indications and timing of this operation use the dynamics of NPi wich determined by pupillometry (NeurOptics, Inc., USA).

Methods: The study was carried out on the NICU of the Regional Vascular Center of Tomsk and included 63 patients with intracranial hemorrhages and two patients with malignant cerebral artery ischemia. The trend of neurological pupillary index was assessed. NPi is an integral index calculated from the latency, the rate of constriction and subsequent dilation, the difference between pupil size after a standardized light stimulus. The norm of its values are in the range of 3.0 to 4.9.A decreasing of NPi below 3.0 was considered as pathological.



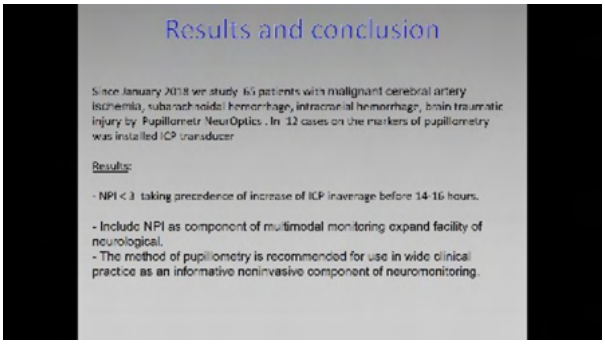
To determine the indication and timing for the install of invasive ICP transducers using the method of pupillometry with NPi-200 device (NeurOptics, Inc., USA).

Results: The analysis of NPi trends has revealed steady decreasing below the level of 3.0 by 12 patients. They received the repeated neuroimaging and surgical treatment with installation of ICP transducer. The level of ICP immediately after surgery was no higher than 20mm. These patients had a steady ICP increase within 12 hours and required dehydrating solution, hyperventilation, decompression.



The study was carried out on the NICU of the Regional Vascular Center of Tomsk and included 63 patients with various forms of intracranial hemorrhages and two patients with malignant cerebral artery ischemia. There is a clinical case of use pupillometry

Conclusion: The dynamics of the NPi is a predictor of ICP increasing by patients with acute cerebral pathology a few hours before its critical rise. Inverse correlation between the NPi dynamics and ICP level was confirmed. The method of pupillometry is recommended for use as an informative noninvasive component of neuromonitoring.



The dynamics of the NPi index is a predictor of ICP increasing by patients with acute cerebral pathology a few hours before its critical rise

Disclosure: Regional Hospital of Tomsk, Siberian State Medical University

EPO-244

A case of acute haemorrhagic leukoencephalitis

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Background and aims: Acute haemorrhagic leukoencephalitis (AHLE) is a rare fulminant demyelinating disease characterised by an acute onset and rapidly progressive encephalopathy. It typically affects young adults and is often associated with a preceding respiratory tract infection.
Methods: We will present the case of a 39-year old Caucasian female with a history of immune thrombocytopenia, who was diagnosed with AHLE.
Results: The patient presented with acute confusion and fever following a three day viral prodrome. On initial examination neck stiffness and expressive dysphasia were noted. Laboratory investigations revealed a pancytopenia, with mildly raised inflammatory markers. Neuroimaging showed extensive vasogenic oedema in the left fronto-parietal region. Intravenous (IV) dexamethasone, ceftriaxone and acyclovir were administered on a suspicion of encephalitis. The patient then developed global aphasia and severe lethargy, with repeat imaging showing an enlarging area of oedema, midline shift and evidence of cortical haemorrhage. These findings were in keeping with the diagnosis of AHLE. IV methylprednisolone, levetiracetam and immunoglobulin were prescribed and the patient's condition was closely monitored. Her neurological status however deteriorated rapidly, requiring IV mannitol and an urgent right decompressive craniotomy. Subsequent management involved IV cyclophosphamide and further supportive measures in an intensive care setting.
Conclusion: AHLE is a life-threatening neurological emergency, with a high mortality rate. Clinical, neuroimaging and laboratory investigations are of a low diagnostic yield in aiding physicians to reach this diagnosis.
Disclosure: Nothing to disclose.

EPO-245

Etiology of status epilepticus in Neurological Intensive Care Unit

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Background and aims: Status epilepticus (SE) is a neurological emergency with various etiology, clinical presentation and unpredictable outcome. Therefore, the aim of our study was to determine whether the etiology of SE could be predictor of its clinical features and outcome.
Methods: Retrospective study included 91 patients with the SE treated in our Neurological Intensive Care Unit (NICU) over a 5-year period. Demographic and clinical characteristics of our patients were obtained from medical data. Regarding etiology patients were divided in five groups: cerebrovascular; poor compliance to antiepileptic therapy (AET); infections (CNS and other); cryptogenic and other causes.
Results: The most frequent cause of SE was infections (36.3%); CNS infection in 6.6% and other infections in 29.7% of patients. Cerebrovascular etiology was registered in 19.8% and poor AET compliance in 18.7%. Etiology was a predictor of seizure semiology ($p<0.01$): 68.75% of patients with SE due to poor AET compliance had generalized tonic-clonic seizure, same as 55.55% of patients with cryptogenic SE. Patients with preexisting epilepsy most commonly had SE due to poor AET compliance ($p<0.01$). In our study mortality was 16.5%. We observed statistically significant association between SE etiology and outcome ($p<0.05$). Survival rate was the highest among patients who had SE due to poor AET compliance.
Conclusion: Infection and cerebrovascular disease were most common cause of SE in our NICU. Etiology of SE was shown to be associated with its clinical presentation, history of preexisting epilepsy and outcome.
Disclosure: Nothing to disclose.

EPO-246

Cardiac arrest, a different reality for neurologists and cardiologists

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Background and aims: Neurologic prognostication is a common topic of discussion between Neurologists and Cardiologists. The objective of this study was to assess the different perspectives of both specialties based on the usual type of patients each specialty approaches.
Methods: 50 patients with cardiac arrest were randomly selected and divided in two groups based on being submitted to two distinct exams from 2017–2019: the "neurology group" with 33 patients, based on doing an electroencephalogram (EEG) and "cardiology group" with 17 patients, based on being submitted do a coronarography.
Results: Patients from both groups have similar baseline characteristics. Patients of the "neurology group" live less, have worse functional prognosis, higher enolase and are more likely to have a tracheostomy. Only one patient from the "neurology group" had a mRS 3. Evoked somatosensory potentials were rarely performed. Almost 50% of the EEGs were performed in the 1st 72 hours. There was no statistically significant difference in the cardiac arrest time/ place, imaging methods, neurology consultation or coronarography between groups.
Conclusion: Neurology doctors have a probably worse perception of cardiac arrest as they are requested to intervene in cases with worse functional outcome, but these doctors should bear in mind that some of these worse patients have a good functional outcome. There should be technical conditions to employ evoked somatosensory potentials in every hospital as this test is fundamental in the neurological prognostication algorithm.
Disclosure: No disclosures.

EPO-247

Efficacy of prophylactic use of haloperidol to prevent delirium in critically ill patients

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Background and aims: Delirium is a complex neuropsychiatric disorder characterized by dysfunctions in cognition and adequate prevention of this disturbance is indispensable to reduce worse outcomes. Our study aims to analyze the efficacy of Haloperidol to prevent delirium in critically ill patients. This antipsychotic is broadly used although there is no consensus on the best form of delirium prophylaxis.
Methods: Our study is a review of literature which includes studies published on the PUBMED platform and Scopus (Elsevier) in the last 10 years, originally in English. The target population includes critically ill patients, especially adults and elderly in the postoperative period. The search strategy used was (haloperidol) AND (delirium) AND (prophylaxis), resulting in 73 articles. Only observational, experimental studies and clinical trials were included and duplicated studies were excluded.
Results: After selection criteria, 15 articles were included for final analysis and the use of this antipsychotic was not effective in 14 of these studies although no significantly adverse effects were noted. Haloperidol did not reduce incidence or severity of delirium in patients acutely admitted in hospital and neither reduced mortality rates or prolonged hospitalization. However, only one article proposed a possible effectiveness of Haloperidol as delirium prophylaxis in elderly patients undergoing esophagectomy.
Conclusion: The majority of these studies did not prove the efficacy of Haloperidol to prevent delirium in critically ill patients, particularly in adults admitted in Intensive Care Units. Therefore, delirium prophylaxis still remains a major clinical challenge.
Disclosure: Nothing to disclose.

EPO-248

Hormonal state dysregulation in patients with chronic disorders consciousness

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Background and aims: Objective is to study gonadotropic, ovarian and thyrotropic functions among patients with chronic DOC.

Methods: We examined nine women with chronic DOC from 20 to 34 years . Etiology of DOC: hypoxia – 6 , TBI – 3; The level of consciousness was determined by the CRS-R scale (x5) : 4 – MCS "plus", 2 – MCS "minus", 3 – unresponsive wakefulness syndrome . The mean duration of DOC 4,72 months. All patients had an oligomenorrhea or amenorrhea, blood hormone levels are determined once a week three times in a row: FSH, LH, estradiol, progesterone, total testosterone, prolactin, TSH and free T4.

Results: Five patients with hypogonadotropic anovulation (FSH level <1.5 IU/L), four – normogonadotropic anovulation. Prolactin levels among seven of patients were within the reference frames, but two of patients with chronic DOC had hypoprolactinemia. It was noticed that two patients had an expressed hypoestrogenemia, when the others had lower limit of normal of estradiol. The values of TSH and free T4 were within the reference range. Endometrial thickness (M-echo) according to pelvic ultrasound examination was from 1 to 3mm.

Conclusion: Understanding of hormonal regulation mechanism disruptions in chronic DOC may open prospects for choosing pathogenetically based hormone replacement therapy and improve outcomes in the form of consciousness recovery

Disclosure: The study is supported by the grant of the RFFR 19-29-01066.

EPO-249

Out-of-hospital cardiac arrest: a retrospective study of clinical outcomes and EEG patterns

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Background and aims: Out-of-hospital cardiac arrest (OOHCA) is associated with high mortality, and a significant proportion of survivors sustain significant hypoxic brain injuries. Accurate identification of patients with favourable neurological outcome in clinical practice is challenging despite the availability of clinical guidelines.

Methods: We examined the outcome of patients presenting with OOHCA in a UK teaching hospital with on-site neuroscience services. Clinical, electroencephalography (EEG), neuroimaging data were analysed retrospectively (study period Nov 2019–March 2020).

Results: 33 patients with OOHCA were identified (25 men; mean age 60 years). Cardiac disease (n=14) was the most common cause of OOHCA, followed by toxic (n=4), neurological (n=3), respiratory (n=3), metabolic (n=2), trauma (n=2) and unknown (n=4). Life support treatment was withdrawn within 24 hours of admission for 11 patients (33%) due to multi-organ failure and significant co-morbidity. 12 patients (36%) had a GCS 14 on sedation weaning. Neurological investigations were performed to guide further management in 10 patients (30%) with a GCS four after sedation weaning; five patients received a maximal dose of anticonvulsant for clinical seizures before EEG. Eight patients who had malignant EEG appearances and hypoxic-ischaemic encephalopathy (HIE) imaging changes died. One patient with benign EEG changes survived with a severe disability while another patient demonstrated good neurological outcome despite diffuse HIE changes.

Conclusion: Our findings showed that approximately a third of OOHCA cases had persistently low GCS after sedation withdrawal and required further neurological assessment. Malignant EEG findings were predictive of poor outcomes.

Disclosure: Nothing to disclose.

Epilepsy 2

EPO-250

Evaluation of Direct Medical and non-Medical Cost of Epilepsy at a Tertiary Neurology Center in Rwanda

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[1] Pharmacy, Kigali, Rwanda, [2] Pharmacy, Kigali, Rwanda, [3] School of Medicine, Leuven, Belgium, [4] Health Economics, Barcelona, Spain, [5] Neurology, Sint-Katelijne-Waver, Belgium, [6] Neurology, Ghent, Belgium

Background and aims: We evaluated the annual direct medical cost (aDMC) and direct non-medical cost (aDnMC) of epilepsy management at the Ndera tertiary hospital (Kigali, Rwanda).
Methods: aDMC was retrospectively calculated upon review of medical records of all persons living with epilepsy (PwE), aged >18 years, and seeking for the first time in 2018 specialist neurology care at Ndera. PwE attended the recommended monthly consultation schedule. Structured interviews were used to determine aDnMC in PwE attending consultation in August 2020.
Results: Mean total aDMC, based on 55 PwEs, was 248,9 US$. Mean aDMC for medical consultations, administration/technical/laboratory investigations combined, hospitalisation and anti-epileptic drugs were 30.7US$, 48.8, 7.6 US$ and 161.7 US$, respectively. Weighted mean biomedical care aDnMC, based on 69 PwE, was 73.0 US$, including round-trip transportation, food, beverage, and accommodation related to the consultation. The Rwandan Community-Based Health Insurance covered medical care for eligible patients with an weighted aDMC of 226.3 US$. Annual Out-of-Pocket (OoP) cost for PwE were 163.3 US$ per year. Over 50% of PwE sought traditional healers' care with a weighted mean and median cost of 67.6US$ and 21.5 US$, respectively. Mean time spend at the hospital and mean travel time both exceeded four hours.
Conclusion: Epilepsy management, measured by DMC, is an important economic burden for PwE and Rwandan health services. OoP DnMC were three times higher than DMC and exclude costs for traditional healers. Indirect costs, including travel and hospital time, were not monetised but equally represented an important burden.
Disclosure: This study was funded by CSR department, UCB Pharma. Peter Dedeken and Paul Boon have recieved consultancy fees from different companies. Other authors have nothing to disclose.

EPO-251

Informative value of routine EEG and nocturnal EEG-video monitoring

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Background and aims: The aim was to study the informative value of routine EEG and nocturnal EEG-video monitoring in adult patients with epilepsy.
Methods: We examined 1,217 patients who were referred to a specialized epilepsy clinic; of those, 589 (48.4%) men and 628 (51.6%) women aged from 22 to 83 years. In these patients, the age of seizure onset varied from one month to 72 years. In total, 915 routine EEG and 302 nocturnal EEG video monitoring were performed.
Results: During the routine EEG procedure, no epileptiform activity was detected in 379 (41.42%) patients. Among other patients, non-epileptic changes were found in 163 (17.81%), focal epileptiform activities in 203 (22.19%), and generalized epileptiform activities – in 170 (18.58%) patients. During the nocturnal EEG-video monitoring, no epileptiform activity was detected in 34 (11.26%) patients; among other patients, non-epileptic changes were found in 11 (3.64%), focal epileptiform activities in 167 (55.3%), and generalized epileptiform activities – in 90 (29.8%) patients.
Conclusion: Routine EEG and nighttime EEG video monitoring do not always reveal an epileptiform activity. The probability of detecting an epileptiform activity is higher with nocturnal EEG video monitoring due to its longer record duration and an increased epileptiform activity in sleep. The probability of detecting an epileptiform activity also depends on the form of epilepsy. It is advisable to gradually replace a routine EEG procedure with a nocturnal EEG-video monitoring.
Disclosure: Nothing to disclose.

EPO-252

The effectiveness of monotherapy in juvenile myoclonic epilepsy

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Background and aims: An objective of the retrospective observational study was to evaluate the effectiveness of juvenile myoclonic epilepsy (JME) monotherapy in long-term follow-up.
Methods: Monotherapy was prescribed for 45 JME patients; average age – 23 years (from 15 to 53). The relative risk (RR) was calculated using RevMan 5.3. Favorable treatment outcome: the number of patients with a complete absence of seizures.
Results: Valproic acid (VA) was used in 71%; topiramate (TPT) – 7%, levetiracetam (LEV) – 22% of patients. The average prescribed daily doses M(SD) VA were 21.4 (2.6), TPT – 2.9 (0.7); LEV – 22.4 (1.8) mg/kg/day. Comparative effectiveness of VA versus TPT after one year of treatment: RR=6.67; 95% CI [0.50, 89.51] p=0.15; two years: RR=6.42; 95% CI [0.48, 86.35] p=0.16; three years: RR=5.94; 95%CI [0.44, 80.01] p=0.18; four years: RR=5.45; 95%CI [0.40, 73.68] p=0.2. Effectiveness of VA versus LEV after one year monotherapy: RR=1.69; 95% CI [0.89, 3.19] p=0.11; two years: RR=2.03; 95% CI [0.93, 4.42] p=0.07; three years: RR=2.50; 95% CI [0.95, 6.58] p=0.06; four years: RR=6.88; 95% CI [1.06, 44.79] p=0.04. During long-term follow-up (4 years or more), patients with three seizures types (myoclonus, generalized tonic-clonic seizures (GTCS), absences) treated by VA were two times more likely to have incomplete seizure control compared to those with only one or two types.
Conclusion: Valproates are more effective in JME treatment than topiramate or levetiracetam. The prognosis for JME in the presence of three types of seizures (myoclonus, GTCS, absences) is worse than in the presence of one or two types.
Disclosure: The reported study was funded by Russian Foundation for Basic Research (RFBR) according to the research project 17-29-09096.

EPO-253

Assessment of auditory verbal memory in children and adolescents with idiopathic generalized epilepsy treated by AEDs

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Background and aims: The side effects of antiepileptic drugs (AEDs) on cognitive functions are recommended to be assessed in idiopathic generalized epilepsy (IGE) as it influences cognitive status minimally. In 2018, the authors worked out Russian-language neuropsychological battery for the assessment of cognitive functions and speech in children and adolescents (&A) treated by AEDs. The abstract presents the results of auditory verbal memory subtests.
Methods: Auditory verbal memory (delayed recall of five words) was assessed in 45 &A (12–17 years old), 15 (with IGE) formed the study group (SG), 30 (without neurological diseases) – the control group (CG). The assessment in SG was conducted before treatment, after 3, 6, 9, 12, 18, 24, 30 months, during the same periods in CG (without treatment). Risk ratios and 95% confidence intervals for unfavorable outcome (UO) were calculated with RevMan5.3 package. UO between SG and CG was compared (results were considered significant when $p<0.05$).
Results: Comparative analysis of results in SG and CG revealed statistically significant difference after 18 months (5 words out of five results decreased): RR=0.32; 95% CI [0.11, 0.90] (p=0,03), after 24 months: RR=0.33; 95% CI [0.12, 0.96] (p=0,04), after 30 months: RR=0.32; 95% CI [[0.11, 0.90] (p=0,03).
Conclusion: The results show mild but constant decline of auditory verbal memory in C&D treated by AEDs after 18 months of treatment. Auditory verbal memory testing should be longitudinal and continued throughout the course of treatment.
Disclosure: The reported study was funded by Russian Foundation for Basic Research (RFBR) according to the research project 17-29-09096.

EPO-254

Hyperglycemia induced global aphasia followed by focal motor seizures as first manifestation of diabetes mellitus

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Background and aims: Hyperosmolar hyperglycemic state (HHT), a life-threatening complication of diabetes mellitus, may initially present with various neurological symptoms. Focal motor seizures are among the most common manifestations whilst aphasia has rarely been described so far.
Methods: We herein report a case of a patient with nonketotic hyperglycemia-induced global aphasia, followed by focal motor seizures.
Results: Brain computerized tomography (CT) scans on presentation and 48 hours later were normal, thus excluding any structural or vascular abnormality, whilst electroencephalography (EEG) did not show epileptiform discharges. Focal seizures subsided with blood glucose management, fluid replacement and antiepileptic treatment. Aphasia resolved gradually, within seven days after admission.
Conclusion: In conclusion, physicians (both neurologists and internists) should be aware of the association between HHT and aphasia, as well as focal motor seizures. Language disturbance, as the initial symptom of hyperglycemia, has rarely been described so far and could lead to poor patients' prognosis if not evaluated early. Prompt diagnosis and immediate management of hyperglycemia and hyperosmolarity, as well as proper anticonvulsant treatment may improve the outcome of HHT patients and avoid unnecessary investigation and inappropriate treatment.
Disclosure: The authors declare that there is not conflict of interest.

EPO-255

Experience in the initiat ion of zonisamide treatment in a secondary hospital.

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Background and aims: Zonisamide is an antiepileptic drug approved in mono and combination therapy for focal-onset seizures. We have evaluated the results after starting this drug in patients in the epilepsy clinic of our center.
Methods: We have analyzed patients treated with zonisamide for at least six months (mean 29.5 months) in the last 10 years in a secondary hospital, obtaining 54 patients, of whom 29 were on monotherapy and 45 presented focal-onset seizures.
Results: Of the 41 patients who presented seizures at the start of treatment with zonisamide, 16 were on monotherapy and 25 were on combination therapy. 51.2% of patients reduced the number of seizures by more than 50% (68.8% vs. 40% p=0.005); 34.14% were free of seizures (68.8% vs. 12% p=0.14); Seizures were reduced by 28.13% (50% vs. 10% p=0.12). The daily equivalent dose was 0.9 and 1 and the two-year follow-up was 68.75% vs. 56% respectively. Side effects were greater in the combination therapy group (60% vs. 37.5% p=0.27). In the adjusted model, the presence of side effects (OR 0.09) and the focal origin of the epilepsy (OR 8.47) reached statistical significance for seizure-free patients.
Conclusion: In our series, side effects were the most important limiting factor for patients to achieve an optimal response. Response rates similar to those described with a high retention rate were obtained from patients who tolerated it. Likewise, the patients who met the indication for focal seizures obtained a better response.
Disclosure: Nothing to disclose.

EPO-256

The efficacy of hormone therapy in after-stroke epileptic spasms

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Background and aims: Aim: to describe some of the clinical features and evaluate the efficacy of hormone therapy in young children with epileptic spasms after pediatric stroke.

Methods: A retrospective prospective study of 10 children with epileptic spasms (ES) (8 boys, two girls) developed after a pediatric stroke.

Results: Hemorrhagic stroke (HS) was in eight children, arterial ischemic stroke (AIS) with hemorrhagic degeneration in 2, respectively. Average age of stroke development – 0.25±1.7 years. The average age of ES development is 0.8±0.4 years. The time since the development of a stroke to the onset of ES was 5.7±5.1 months (6 months – eight children). Hypsarrhythmia was found in five children, four of them had a zone-accentuated variant. eight out of 10 children received a starting course of steroids (5 prednisolone, two hydrocortisone acetate, one dexamethasone). The effectiveness of steroids against spasms and/or hypsarrhythmia was 88%. The onset of the effect was 6.3±21.9 days. Follow-up: relapse of epilepsy with focal seizures happened in seven patients, six of them experienced multifactorial medical intractability. The median relapse was seven months. Four patients are in remission on the use of AEDs, the average duration of remission is 2.6±1.2 years.

Conclusion: After-stroke ESs in all children were associated with hemorrhagic brain damage and occurred (80%) in the first six months after pediatric stroke. The use of steroids showed an extremely high (88%) and rapid effect in suppressing after-stroke ES. However, later there was a transformation into medical intractable focal epilepsy in the majority (60%) of children.

Disclosure: Nothing to disclose.

EPO-257

Third generation aeds in the elderly: use of perampanel in pharmacorresistant epilepsy

M.J. Hernandez Garcia [2], G. Dionisio [1], L. Iacampo Leiva [3], G. González Toledo [1], C. Hernández Javier [2], M. Crespo Rodríguez [1], M. Lobato González [1], F. Carrillo Padilla [1]

[1] Neurología, Spain, [2] San Cristobal de La Laguna, Spain, [3] Tacoronte, Spain

Background and aims: Epilepsy is a prevalent condition in elderly patient (134/100,000). Its management is usually affected by concomitant diseases and polypharmacy. Third-Generation AEDs (TG-AEDs) are the last AEDs marketed, with a better profile of interactions and less secondary effects than previous AEDs.

Methods: We reviewed the medical records of patients older than 60 years old assessed in our Epilepsy Clinic between January-December 2019.

Results: 98 patients were enrolled, 39.7% patients received one or more TG-AEDs: Eslicarbazepine (11), Lacosamide (22), Perampanel (18) and Brivaracetam (7). We analyzed patients treated with PER: 55% women, mean age 67 years (60–79). Mean time from onset: 38 years (2–64). 94% focal onset seizures. 50% structural etiology. Mean AEDs: three (1–5), with 77.8% of the patients taking three AEDs, one monotherapy. Median PER dose: 6mg. 72% showed an improvement in frequency of the seizures: three patients were seizure-free and two had >50% reduction. Adherence was good with only one patient discontinuing PER. Adverse effects: six patients referred worsening gait (3 with a non-complicated fall) and two showed irritability without aggressiveness. 39% of the patients had psychiatric comorbidities. 44% had cognitive impairment, without progression related to PER.

Conclusion: Despite its advantages, the use of TG-AEDs is still low in elderly patients with pharmacorresistant epilepsy. In our series, PER was well-tolerated even in polytherapy with 72% of patients improving seizures frequency, without cognitive or behavioral decline associated. Although further studies are necessary, PER could be a safe and effective option in these patients.

Disclosure: Nothing to disclose.

EPO-258

Atypical Postictal Syndrome (PIS): a case report and literature review

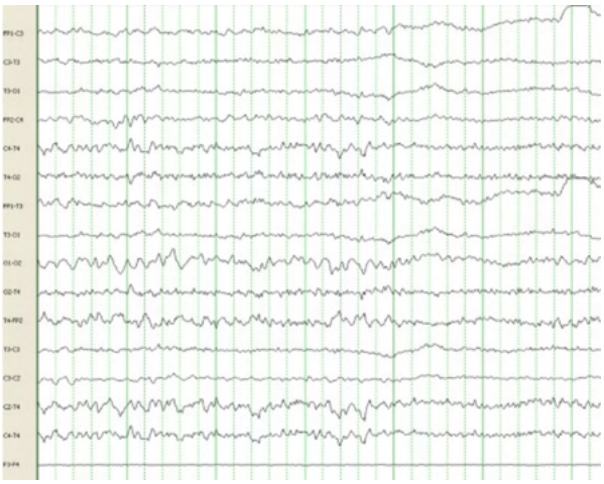
M.J. Hernandez Garcia [2], G. Dionisio [1], M. Villar Martínez [4], L. Iacampo leiva [3], G. González Toledo [1], C. Hernández Javier [2], M. Crespo Rodríguez [1], M. Lobato González [1], F. Carrillo Padilla [1]

[1] Neurología, Spain, [2] San Cristobal de La Laguna, Spain, [3] Tacoronte, Spain, [4] London, Spain

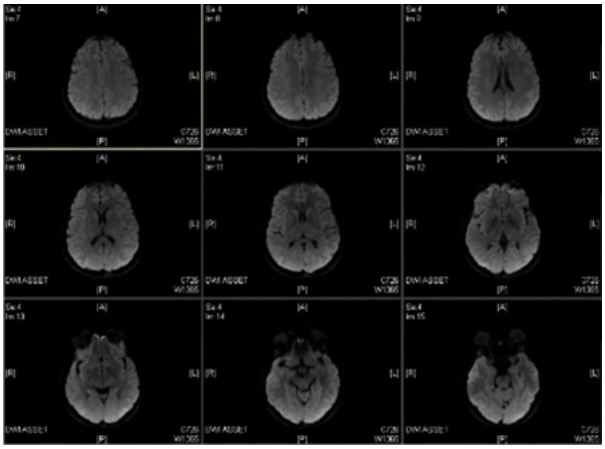
Background and aims: Transient focal signs starting after the ending of an epileptic ictal discharge that are not related to any underlying damage of the CNS are called postictal paresis. They tend to resolve spontaneously in a short period of time, usually less than 36 hours.

Methods: We present a 42-year-old woman with personal history of well-controlled right temporal lobe epilepsy that is found unresponsive. No previous episodes of ictal paresis.

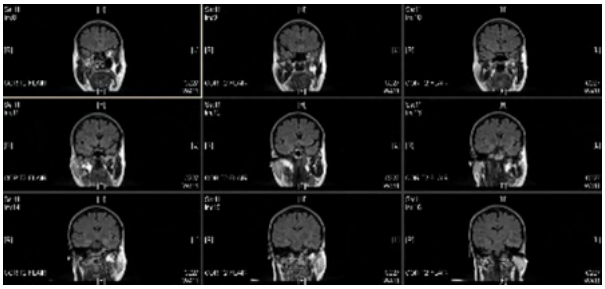
Results: Initial neurological exam revealed somnolence, global aphasia and right side moderate hemiparesis with conjugated gaze deviation to the left side (NIHSS 17 points). Stroke code was activated and brain CT and CT-angiography were normal. Thrombolysis and thrombectomy were not indicated due to the unknown time of onset and the absence of large vessel occlusion. Blood tests showed high serum creatine kinase levels (7,367 U/L; reference range 12–190) and leucocytosis (16,380/mm3). An urgent EEG ruled out status epilepticus (fig 1). Brain MRI-MRA performed in the first 24 hours showed no evidence of acute ischemic lesions (fig 2–3). Domiciliary AEDs treatment was kept and patient showed a progressive recovery, being asymptomatic at day 6.



Urgent EEG on admission: Depressed activity in left hemisphere, with no epileptic activity.



Brain MRI on first day of onset: DWI sequence showing no acute ischemic lesion



Brain MRI on first day of onset: Coronal FLAIR T2 sequence showing no ischemic lesions

Conclusion: Postictal paresis diagnose can be complicated, specially when the symptoms are severe or prolongued in time. Differential diagnosis with non-convulsive status epilepticus and neurovascular events is essential to avoid inappropriate treatment and aggressive management, It's important to document background and relevant clinical signs in addition to keeping a carefully expectant attitude.

Disclosure: Nothing to disclose.

EPO-259

Differential diagnosis of seizures in Klinefelter's syndrome

C. Hernández Javier [2], G. Dionisio [1], M. Hernandez Garcia [2], G. González Toledo [1], M. Crespo Rodríguez [1], M. Lobato González [1], F. Carrillo Padilla [1]

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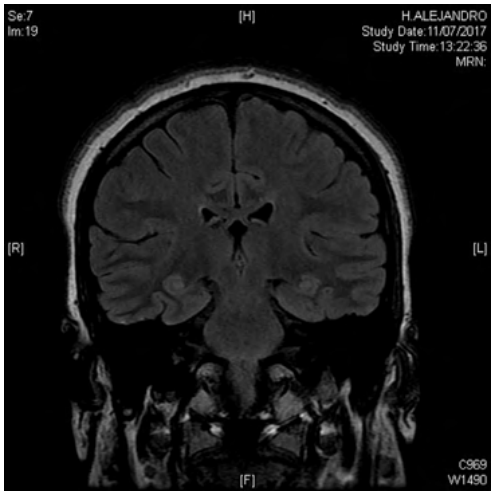
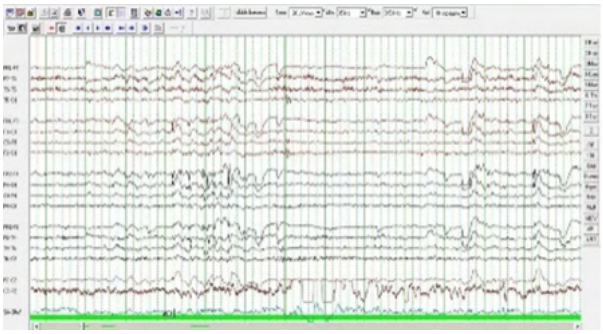
Background and aims: Association between Klinefelter and epilepsy presents a heterogeneous electroclinical spectrum, usually related to generalized epilepsy (GE). Focal onset signs in GE can induce misdiagnose and failed management.

Methods: We introduced a 17-year-old male with childhood febrile seizures, that started at 13 with episodes of fixed gaze and disconnection, facial clonics, fall and tonic-clonic progression. He was started on topiramate and lamotrigin, but due to inefficacy oxcarbazepine was associated, although seizures persisted.

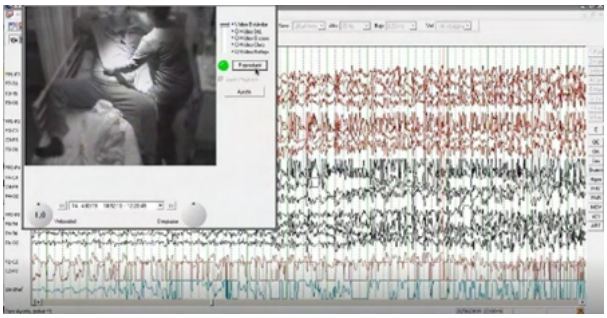
Results: Neurological examination was normal, with characteristic phenotype. Kariotype: Klinefelter syndrome. Blood test: IgA and IgM deficiency, positive c-ANCA, and hormonal disorder. MRI FLAIR-sequence: slight increased signal in bilateral unchal and hippocampal regions. EEG (1): Right temporal slow spike-waves. EEG (2): Left temporo-parietal and right temporo-occipital slow wave. An Autoimmune Focal temporal lobe epilepsy was diagnosed and Ig were started, increasing oxcarbazepine and associating Levetiracetam. Seizures persisted and a VEEG was performed that showed frequent 2–3 seconds generalized interictal discharges with 3–4 Hz spike-waves activity, in wakefulness and sleep. Two generalized 80-second tonic-clonic attacks, compatible with generalized epilepsy. With these results, oxcarbamacepine was discontinued and switched to valproic acid and seizures improved.



MRI (Flair sequence): slight increase signal in bilateral unchal and hippocampal region.



EEG: Left Temporal Spikes.



VEEG: generalized activity, 80-second tonic-clonic attack.

Conclusion: Klinefelter's Syndrome most common semiology is generalized seizures. In our case, Kariotype and VEEG allowed successful diagnosis and treatment. We should be aware that focal signs of onset as well as MRI images, could induce misdiagnose and pharmacoresistance in GE. VEEG remains the essential test for differential diagnosis, allowing to optimize treatments and improve prognosis.

Disclosure: The authors declare no conflicts of interest.

EPO-260

Anticonvulsant Effects of Differentiated Kv7 Channel Potentiator XEN1101 in Combination with Common Anti-Seizure Drugs

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[1] Biology, Burnaby, Canada, [2] Drug Discovery, Burnaby, Canada, [3] Scientific Affairs, Burnaby, Canada, [4] Strategy and Innovation, Burnaby, Canada, [5] Translational Drug Development, Burnaby, Canada, [6] Translational Development, Burnaby, Canada, [7] Clinical Science, Burnaby, Canada, [8] In Vivo Pharmacology, Burnaby, Canada, [9] Biology, Vancouver, Canada

Background and aims: XEN1101 is a positive allosteric modulator of Kv7 channels being developed for epilepsy. Combination of anti-seizure drugs (ASD's) is common in clinical practice.
Methods: The efficacy of XEN1101 was evaluated in combination with valproic acid, phenytoin, or levetiracetam in the direct current maximum electroshock seizure assay (DC-MES). The combined efficacy of XEN1101 and levetiracetam was also evaluated in the 6 Hz psychomotor seizure assay (6Hz).
Results: A weakly efficacious dose of phenytoin (2mg/kg, 25% effective) was combined with XEN1101 at 0.75, 1, 1.5, and 2.5 mg/kg in the DC-MES. The 50% effective plasma concentration (EC50) of XEN1101 alone was 0.154 microM and 0.04 microM when dosed with phenytoin, (3.9X improvement). We next tested a weakly efficacious dose of XEN1101 (1mg/kg, 30% effective) combined with 30, 56, or 100mg/kg valproic acid in the DC-MES. Valproic acid alone had an EC50 of 1,440 microM and 608 microM when dosed in combination with XEN1101 (2.4X improvement). Levetiracetam is ineffective in the MES, but effective in the 6Hz. We combined levetiracetam with XEN1101 in both the DC-MES and the 6Hz. In the DC-MES adding levetiracetam (150mg/kg, 25% efficacy) did not markedly increase the effect of a modest dose of XEN1101 (1.5mg/kg, 38% efficacy versus 50% efficacy with levitiracetam). In contrast, in the 6Hz assay, combining weakly efficacious doses of XEN1101 (4mg/kg, 7% protection) and levetiracetam (300mg/kg, 12% protection) did increase efficacy (67% protection).
Conclusion: XEN1101 improved seizure protection when combined with three ASD's in mouse models.
Disclosure: All authors are employees of Xenon Pharmaceuticals, Inc.

EPO-261

Ictal asystole in long term video EEG; semiology, localisation and intervention. Ten cases report

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[1] Cairo, Egypt, [2] Department of Neurology, Dublin, Ireland

Background and aims: Ictal arrhythmias are disturbances of cardiac conduction that occur during clinical or electrographic seizures. Ictal asystole (IA) is rare, and its incidence can range from 0.3–0.4% in patients with epilepsy who were monitored by video EEG (van der Lende et al., 2015).
Methods: We report on 10 patients (6 males and four females) with an age range (31–70 years old) who were monitored in our video EEG (VEEG) unit over the last eight years. These patients were selected based on the history of documented ictal asystole during inpatient VEEG monitoring).
Results: In our series, the mean latency from the seizure onset to the onset of ictal asystole was 22 seconds and the mean duration of the IA was 15.8 seconds. During the asystolic phase, the seizures may clinically continue or syncopal signs may supervene. In our case series, all the patients had either left or right temporal lobe epilepsy, six of which were lesional. We found two patterns of ictal semiology in our series. The first group of patients included five patients who experienced a rapid onset of IA in their seizure and the second group where the latency of ictal asystole was relatively late.
Conclusion: The manifestation of syncope was more likely present in the late-onset group. All our cohort had a permanent pacemaker following the diagnosis, six of these patients reported no further syncope to date reducing the risk of falls and injuries which were prominent features in two of our patients.
Disclosure: Nothing to disclose.

EPO-262

Epilepsy in patients with anti-MOG syndrome

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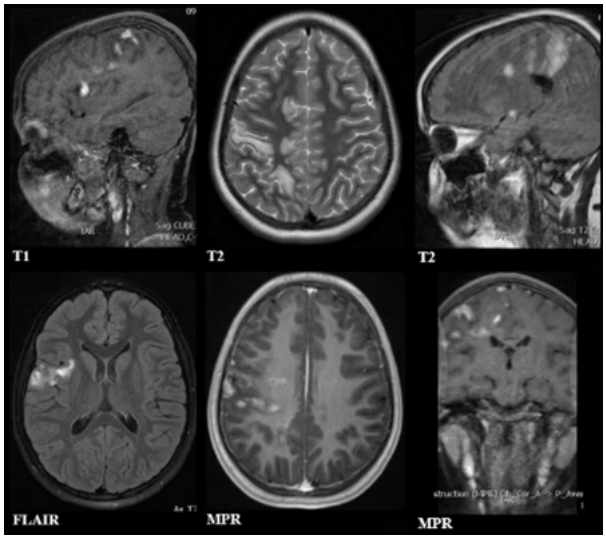
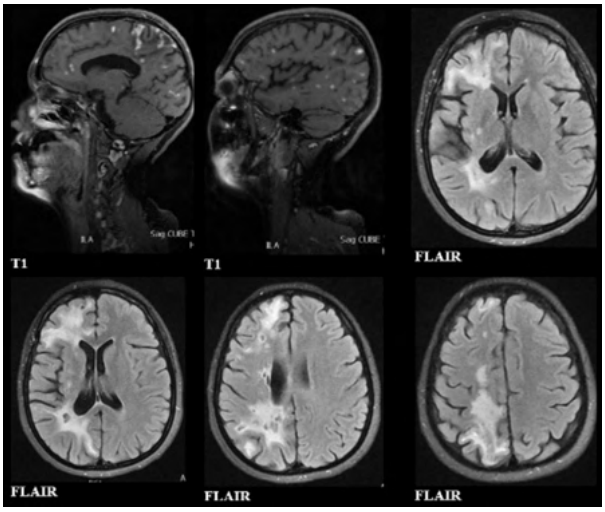
[1] *Neurology, Moscow, Russian Federation*

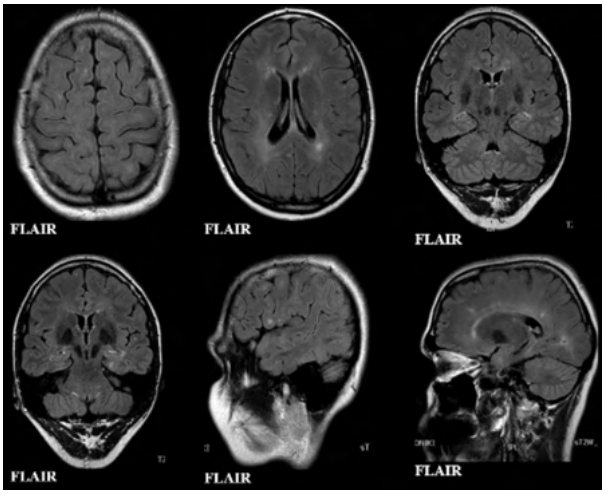
Background and aims: The anti-MOG syndrome (anti-myelin-oligodendrocyte glycoprotein) is a group of demyelinating diseases of the central nervous system in which antibodies attack glycoproteins on the outer membrane of oligodendrocytes (MOG). The aim of the research was to study the course of the disease in patients with anti-MOG syndrome with epilepsy.
Methods: We observed 11 patients (five men and six women) with anti-MOG syndrome aged two months to 46 years. Three patients among them had epileptic seizures, they all were female.
Results: We present three clinical cases in which patients with anti-MOG syndrome had epileptic seizures. In the first patient, epileptic seizures preceded the diagnosis of anti-MOG syndrome. In the second patient, the disease debuted with right-side optic neuritis, seven years later epileptic seizure developed (after childbirth, during which the BBB could become permeable to circulating antibodies to MOG). In the third patient, the disease debuted with headaches. After the acute respiratory viral infection optic neuritis and ataxia appeared. Myelitis was diagnosed. One year later an epileptic seizure occurred. This patient had a combination of CADASIL syndrome with anti-MOG syndrome.



Brain MRI of the patient 1. She had focal sensory epileptic seizures with intact awareness. A year before this MRI, the girl's left leg, left arm became sharply numb. This MRI was performed after new episode of weakness, numbnes in the left leg



MRI of the brain of the patient 2 after five years from the onset of epilepsy. MRI was done when seizure appeared after 1.5 years of seizure absence



MRI of the brain of the patient 3 when myelitis was detected

Conclusion: Epileptic seizures in patients with anti-MOG syndrome are frequent. In addition to antiepileptic therapy, anti-MOG syndrome should be treated. Under this condition, seizures are well controlled and generally have a favorable prognosis.
Disclosure: The authors declare no conflict of interest. The study was performed without external funding. Informed consent was obtained from all patients for being included in the study.

Headache and Pain 2

EPO-263

Migraine secondary to cardiac catheterization

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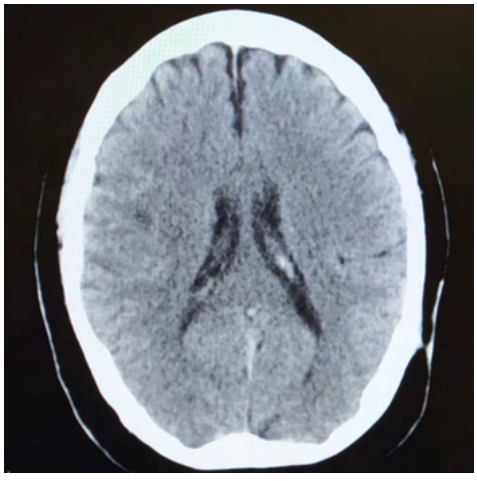
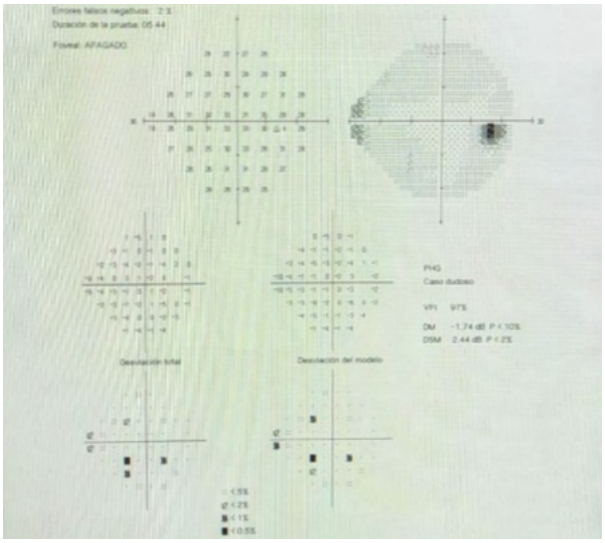
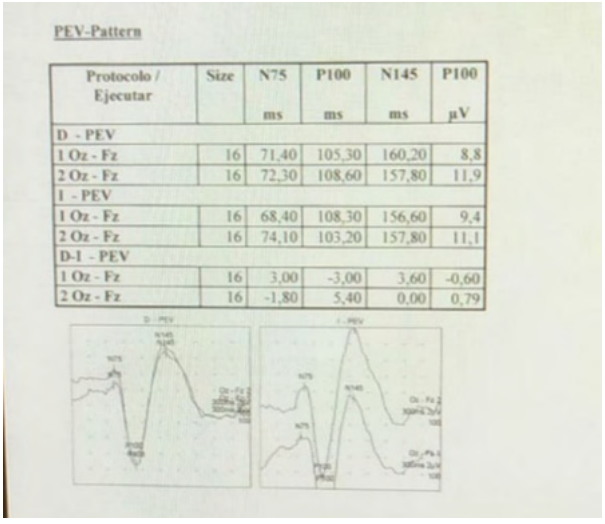
Background and aims: Headache is an exceedingly common symptom that affects virtually everyone at some time in their life. It is estimated that nearly half of the world's adult population has an active headache disorder. Migraine is a collection of symptoms that may include headache, malaise, nausea, vomiting, hypersensitivity to several modes of sensory input (light, sound smell), and often disquieting focal neurological symptoms. Headache disorders are classified as primary or secondary. The primary headache disorders do not have an underlying structural cause, but all the primary headache disorders can be stimulated by secondary conditions.
Methods: This is a 58-year-old, right-handed male patient. He commented as a history of headache with visual aura: scintillating scotoma, with two unique self-limited episodes, 24 and eight years ago, both after performing cardiac catheterization for coronary heart disease. In 2020, he was admitted for a coronary study, presenting after performing the same scintillating scotoma-like visual aura with subsequent pulsatile bifrontal headache that resolved in a few hours.
Results: The following were performed: complete analysis, head CT, brain MRI, visual evoked potentials and campimetry, which were normal. The patient was asymptomatic within a few hours. A follow-up was carried out months later, without the patient presenting new symptoms or any neurological focus. Was diagnosed as: Seconndary Headache: EPO-263 Migraine secondary to cardiac catheterization or attributed to a substance or its withdrawal.



Normal MRi



Normal campimetry



PEV-Pattern

Protocolo / Ejecutar	Size	N75 ms	P100 ms	N145 ms	P100 µV
D - PEV					
1 Oz - Fz	16	71,40	105,30	160,20	8,8
2 Oz - Fz	16	72,30	108,60	157,80	11,9
I - PEV					
1 Oz - Fz	16	68,40	108,30	156,60	9,4
2 Oz - Fz	16	74,10	103,20	157,80	11,1
D-I - PEV					
1 Oz - Fz	16	3,00	-3,00	3,60	-0,60
2 Oz - Fz	16	-1,80	5,40	0,00	0,79

Normal visual evoked potentials

Conclusion: In certain situations, although the triggering cause of the migraine seems clear, the demonstration of it is complex. The medical history is the main tool in the diagnosis of migraine.
Disclosure: Nothing to disclose.

EPO-264

The SQUARE study population: Patient characteristics of erenumab-treated patients in a real-world setting in Switzerland

E. Schäfer [2], I. Meyer [1], M. Arzt [2], A. Gantenbein [3]
[1] *Novartis Pharma Schweiz AG, Rotkreuz, Switzerland,*
[2] *Rotkreuz, Switzerland,* [3] *Bad Zurzach, Switzerland*

Background and aims: In pivotal clinical trials, safety and efficacy of erenumab were demonstrated in patients with episodic and chronic migraine. In 2018, erenumab received Swiss marketing authorization for the prevention of migraine in adults. However, real-world data evaluating the effect of erenumab in a setting of routine medical care are missing.
Methods: SQUARE (CAMG334ACH01) is a non-interventional study aiming to observe the effects of erenumab on quality of life and disability, treatment satisfaction and persistence in a post-marketing setting in Switzerland. In accordance with reimbursement requirements, patients completed migraine diaries for three months prior to erenumab initiation, as well as during therapy.
Results: This study included 174 patients, of which the majority were women (84.9%) with a mean age of 44.2± 13.9 (SD) years. Patients had 16.6±7.2 monthly migraine days and 11.6±7.0 monthly acute migraine-specific medication days at baseline. They had failed (or had contraindications for) 4.0±1.9 prior prophylactic treatments (mostly, beta-blockers or topiramate). The averaged HIT-6™ score at baseline was 65.9±4.9 points. A high proportion of patients had severe disability equivalent to MIDAS grade IV. More than 75% of patients had an IMPAC grade of three or 4, indicating severe or very severe impact on their partners and adolescent children.
Conclusion: This first interim analysis of baseline data exposes a high burden of migraine in patients seeking to initiate erenumab treatment. Subsequent data from this and other studies will evaluate the effect of erenumab in the real-world setting.
Disclosure: Novartis Pharma Schweiz AG funded this study. Erenumab is co-developed by Amgen and Novartis. A detailed disclosure from each author will be included in the oral/poster presentation.

EPO-265

Migraine with pleocytosis, an underdiagnosed disorder

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Neurology, Murica, Spain

Background and aims: In the diagnosis of a headache, we can find neurological deficits that make it necessary to expand the etiological study, being one of the tests to perform the lumbar puncture (LP). An altered cerebrospinal fluid (CSF) can lead us to error if we do not take into account the existence of the condition called transient headache syndrome with CSF lymphocytosis or pseudomigraine with pleocytosis. We present a case of difficult diagnosis.
Methods: We present a 33-year-old man, with no relevant history, smoker and gambler, who came to the emergency room for behavioral alteration of 48 hours of evolution and throbbing holocranial headache, with no other neurological focus. He has been recently admitted with a discharge diagnosis of migraine with aura and imaging tests with no findings.
Results: LP was performed in the emergency department due to suspected encephalitis, finding leukocytosis, being the pacient afebrile. Treatment with acyclovir and analgesia was started, leaving him asymptomatic in two days. The study was completed with imaging tests, serologies and viral PCRs in CSF and EEG, without findings.
Conclusion: Migraine with pleocytosis is a condition unknown by most general practitioners and underdiagnosed by neurologists since LP is not a test that is routinely performed in the study of headaches. It is important to take this into account when making the differential diagnosis of viral encephalitis, giving us the definitive diagnosis the normality of the complementary tests (with no other findings than pleocytosis) and the evolution of the episode.
Disclosure: Nothing to declare.

EPO-266

Pooled analysis of the timing and location of injection-site adverse events with fremanezumab in patients with migraine

D. Holle-Lee [1], Y. Kessler [2], V. Ramirez-Campos [7], X. Ning [3], J. Cohen [4], S. Barash [5], T. Jürgens [6]
[1] Essen, Germany, [2] Israel, [3] Frazer, United States, [4] West Chester, United States, [5] United States, [6] Rostock, Germany, [7] Pescara, Italy

Background and aims: Fremanezumab, a fully-humanized monoclonal antibody (IgG2a) that selectively targets calcitonin gene-related peptide (CGRP), has demonstrated efficacy and tolerability for migraine preventive treatment in three randomized, double-blind, placebo-controlled phase three trials (HALO chronic migraine [CM], HALO episodic migraine [EM], and FOCUS). This pooled analysis of data from those three studies evaluated timing and location of injection-site adverse events (AEs), the most common AEs reported in clinical trials of fremanezumab.
Methods: Across all three studies included in this pooled analysis, patients were randomized (1:1:1) to quarterly fremanezumab, monthly fremanezumab, or matched placebo for 12 weeks of double-blind treatment. The timing and location of injection-site AEs were summarized descriptively.
Results: This pooled analysis included 2,842 patients. In the quarterly fremanezumab (n=943), monthly fremanezumab (n=954), and placebo (n=945) groups, respectively, injection-site AEs were reported for 37%, 37%, and 31% of patients, most commonly pain (22%, 20%, and 20%), induration (15%, 18%, and 13%), and erythema (16%, 15%, and 12%). These AEs were most common within <1 month of initiating study treatment (Table 1). With quarterly fremanezumab, monthly fremanezumab, and placebo, injection-site AEs were more common in the limb than in the abdomen (Table 2).

Table 1. Timing of Injection site AEs

Time category Injection-site AE, n (%)	Quarterly fremanezumab	Monthly fremanezumab	Placebo
<1 month	*(n = 943)*	*(n = 954)*	*(n = 945)*
Injection-site pain	173 (18)	162 (17)	152 (16)
Injection-site induration	126 (13)	117 (12)	96 (10)
Injection-site erythema	131 (14)	110 (12)	91 (10)
1–<2 months	*(n = 936)*	*(n = 948)*	*(n = 936)*
Injection site pain	85 (9)	87 (9)	79 (8)
Injection-site induration	35 (4)	76 (8)	48 (5)
Injection-site erythema	30 (3)	46 (5)	38 (4)
2–<3 months	*(n = 923)*	*(n = 927)*	*(n = 904)*
Injection site pain	51 (5)	71 (8)	55 (6)
Injection-site induration	28 (3)	67 (7)	37 (4)
Injection-site erythema	20 (2)	37 (4)	28 (3)
>3 months	*(n = 754)*	*(n = 744)*	*(n = 781)*
Injection-site pain	2 (<1)	0	1 (<1)
Injection-site induration	3 (<1)	1 (<1)	1 (<1)
Injection-site erythema	2 (<1)	3 (<1)	1 (<1)

AEs, adverse events.

Table 1. Timing of Injection-site AEs

Table 2. Injection-site AEs by Injection Location

Injection location Injection-site AE, n (%)	Quarterly fremanezumab (n = 943)	Monthly fremanezumab (n= 954)	Placebo (n = 945)
Limb			
Injection-site pain	166 (18)	162 (17)	153 (16)
Injection-site induration	132 (14)	159 (17)	107 (11)
Injection-site erythema	121 (13)	117 (12)	84 (9)
Abdomen			
Injection-site pain	89 (9)	81 (8)	78 (8)
Injection-site induration	36 (4)	48 (5)	42 (4)
Injection-site erythema	64 (7)	55 (6)	53 (6)

AEs, adverse events.

Table 2. Injection-site AEs by Injection Location

Conclusion: In this pooled analysis including >1,800 patients receiving fremanezumab, the most common AEs were injection-site AEs, which occurred most frequently in the limb and during the first month of treatment.
Disclosure: These studies and analyses were funded by Teva Pharmaceuticals.

EPO-267

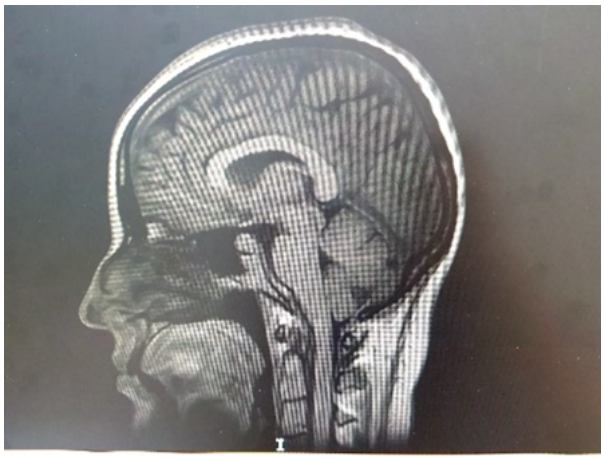
Secondary headache caused by a postraumatic cerebrospinal fluid fistula (CSF-F) in a pregnant patient

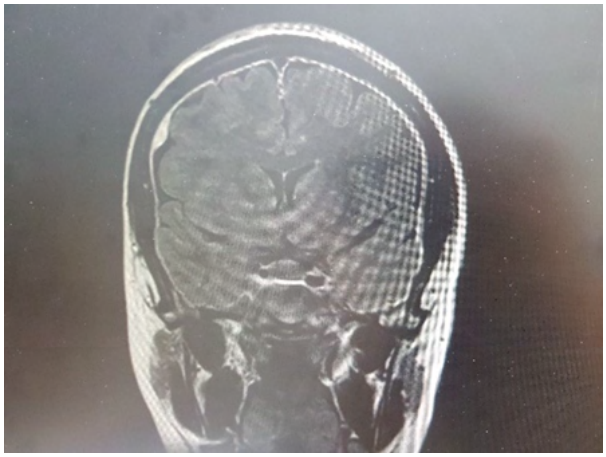
P. Ioan [2], A. Ribigan [1], R. Badea [1], O. Ioghen [1], A. Ciocan [2], C. Bunea [1], F. Antochi [1], I. Mihaela Roxana [2]

[1] Pediatric Neurology, Bucharest, Romania, [2] Neurology, Bucharest, Romania

Background and aims: Cerebrospinal fluid fistulas (CSF-Fs) represent a rare pathology that may appear anywhere in the cranio-spinal tract and are divided into spontaneous and posttraumatic (PT). A category of patients with PT CSF-Fs may present late-onset leakage, 8–30 days after the traumatism.

Methods: We present the case of a 31-year-old pregnant female patient (first trimester) with diffuse newly onset moderately-severe headache, vertigo, nausea and vomiting, aggravated by orthostatism. six weeks prior, she had an episode of left tinnitus and otalgia and two weeks later received a blow to the left ear. The cerebral MRI showed a 35 degree pontine-mesecephalic angle, drooping splenium of corpus callosum, bilateral subdural hematomas and a T2 left mastoid hyperintensity suggestive of a small CSF-F. Fibroscopy revealed left ear CSF leakage.





Results: In order to preserve the pregnancy, we proposed conservatory treatment. Repeated fibroscopic examination noted the absence of CSF-F leakage and subsequent clinical and imagistic improvement.

Conclusion: The otalgia and tinnitus perceived by the patient prior to the traumatism were, probably, generated by an undiagnosed left ear/nasopharinx inflammatory pathology, which might have predisposed towards developing a CSF-F. It is noteworthy that four weeks passed between the traumatism and the onset of symptoms. Although most fistulas close within 48 hours, in this case it persisted for four weeks. Usually, persistent CSF-F require surgical closure but, in this case, to preserve the pregnancy, a surgical intervention carried too much risk. A prolonged conservatory treatment was able to lead to CSF-F closure after four weeks, with an optimal outcome.

Disclosure: Nothing to disclose.

EPO-268

Treatment options in management of neuropathic pain : when to associate?

M. Jamoussi [3], H. Jamoussi [3], S. Athimni [1], H. Essoussi [1], S. Khalbous [1], M. Kolsi [1], R. Friaa [1], E. Cheour [1], M. Fredj [2]

[1] Pain management center, Rabta hospital, tunis, Tunisia, [2] Neurology department Charles Nicolle Hospital, Tunis, Tunisia, [3] Tunis, Tunisia

Background and aims: Neuropathic pain is a major health problem (with a prevalence up to 8%) with an impact on the quality of life and on the economy. We attempted to judge the impact of drug-associations in chronic neuropathic pain.
Methods: A retrospective and analytic study in a tertiary pain management center in Tunisia including patients consulting for neuropathic pain from January 1st 2019–2020. Patients with a follow up of more than six months were included in the analytic study. Pain was evaluated with the Visual analog scale and treatment was considered effective for >50% of pain relief.
Results: 213 patients, sex ratio=0,88. Mean age 57.58±13.99. 35.2% were diabetic. Most common aetiologies: painful diabetic neuropathy (16.5%), post-herpetic neuropathy (29.6%), common radiculopathies (25.8%), trigeminal neuralgia (10,8%) and vertebral metastases (7%). 152 patients had a regular follow up. Associations were indicated in 71% (among which 22.9% on 3-therapy) mostly for mixed pain (46,8%) or unsufficient anlgesia (21.1%). first line dual therapy was not superior to monotherapy (p=0.611). Tramadol-1st line dual-therapies proved to be efficient within the first 3–6 months (p=0.035; p=0.037) but not for longer (p=0,27). 3-therapy including tricyclic antidepressants, pregabalin and tramadol was only efficacious in the first three months (p=0.004). Overall >50% pain relief was achieved for 56.6%. Gender, age and diabetes had no influence on pain relief (p=0.249; p=0.564; p=0.134).
Conclusion: Management of neurpathic pain should be adjusted upon the underlying diagnosis. Mixed pain is usually underdiagnosed. The early association of an opoïd is usufel in this case.
Disclosure: No disclosures

EPO-269

Clinical Significance of Diagnostic Delay in Patients with Cluster Headache

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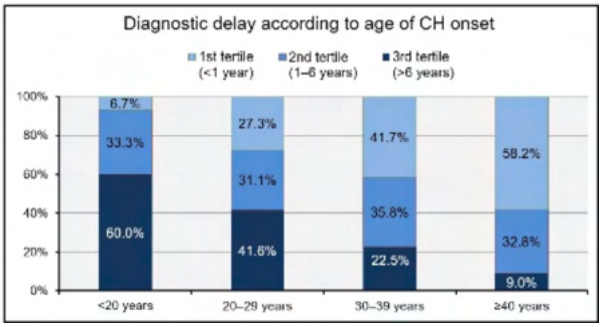
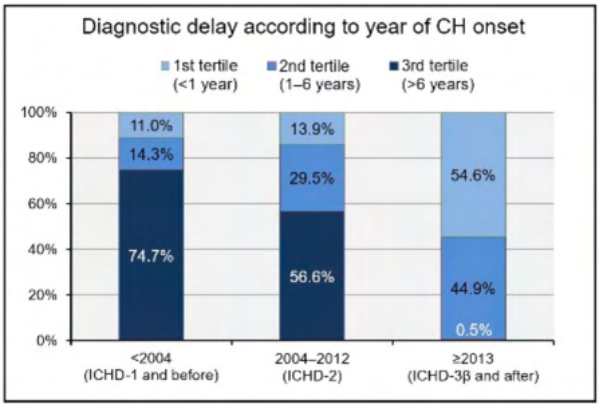
Background and aims: To investigate diagnostic delay of cluster headache (CH) and its clinical influence in Korean patients.
Methods: We analyzed data from the Korean Cluster Headache Registry, a prospective multicenter registry of 15 hospitals, diagnosed with the ICHD-3.
Results: Of 453 eligible patients, mean duration of diagnosis delay was 5.6±6.6 years, ranging from 0 to 36 years (tertiles of diagnostic delay: first tertile, <1 year; second tertile, 1–6 years; and third tertile, >6 years). Regarding age of CH onset, the proportion of the 3rd tertile was the highest for the youngest age group (<20 years), but the lowest for the oldest age group (>40 years; 60.0% vs. 9.0%; and p< 0.001). In terms of the year of onset, the proportion of the third tertile was the highest for the group of CH onset before 2004 (the publication year of the ICHD-2), but the lowest for the group of CH onset after 2013 (the publication year of the ICHD-3 beta version; 74.7% vs. 0.5%; and p<0.001). There was no difference between the tertile groups, in terms of CH characteristics, anxiety/depression scores and headache impact (the 6-item Headache Impact Test).



Diagnostic delay according to age of CH onset



Diagnostic delay according to year of CH onset and ICHD publication

Conclusion: In line with previous findings, younger onset CH patients and the patients with CH onset in the era of previous ICHD experienced longer diagnostic delay, supporting the clinical significance of better headache education and disease awareness to reduce the burden of CH.
Disclosure: Nothing to disclose.

EPO-270

More Than a Headache

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Background and aims: In the daily clinical practice of a family doctor, complaints associated with chronic pathology often arise. However, this symptom can sometimes mask a more serious clinical condition.
Methods: A 59-year-old female patient is presented. Relevant personal history: lumbar osteoarticular pathology confirmed by CT scan, with about 10 years of evolution. She goes to the consultation referring sensation of a "stuck leg" on the left, without pain, but that made it difficult to walk, with about one month of evolution. After using our consultation several times, and after a variety of complementary diagnostic tests, brain MRI revealed a space-occupying lesion at the intraventricular level. the lesion was excised, and the histology revealed a grade IV glioblastoma, with parieto-occipital location in the right side.
Results: During the post-surgical reevaluation consultation, the patient revealed that, in the context of an accidental TBI in 2009, she underwent an MRI scan where a suspicious lesion with an "epileptic focus" was visible, with the hypothesis that it was a low-grade glioma.
Conclusion: When symptomatology is persistent, it is essential to exclude the most common and known causes, but we must never forget any less frequent pathologies that require more in-depth and targeted investigation.
Disclosure: Nothing to disclose.

EPO-271

Neuropsychological deficits and neuropsychiatric outcomes in chronic migraine

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Background and aims: The aim of the present study was to assess the presence of neuropsychological impairment (NI) in patients diagnosed with chronic migraine (CM), and explore its association with clinical and neuropsychiatric outcomes.
Methods: We enrolled 36 patients with CM (33 women, average 45 years old) during headache-free period, and 18 age-, gender-, and education level- matched healthy controls (HC) in a case-control study. All participants underwent a full clinical and neuropsychiatric examination and a comprehensive neuropsychological test-battery. Independent group t-test and multiple regression analysis were performed to respectively determine differences between groups and the predictive value of the assessed measures in cognitive performance.
Results: CM patients exhibited poorer scores for all clinical neuropsychiatric measures, mainly for depression and trait-anxiety. No statistical differences were found for personality traits. Compared to HC, CM patients exhibited a significantly larger Stroop interference effect, with the rest of neuropsychological measures showing no differences. Nevertheless, and taking into account the number of failed tests, 42% of CM patients showed absence of NI, whilst mild to moderate NI was presented in 45% of them. Verbal and visuo-spatial episodic memory, planning ability, and executive control were the most frequently impaired cognitive domains. Importantly, the Migraine Disability Assessment Scale (MIDAS) was the single variable retained in regression model predicting global neuropsychological performance in MC patients.
Conclusion: The presence of cognitive and neuropsychiatric dysfunction is a subtle but a relevant consequence in CM patients during headache-free period whereas neuropsychological performance may be moderately predicted by headache-related disability.
Disclosure: Supported by: Spanish RYC-2015-18467 grant.

EPO-272

When chronic migraine remains refractory: can anti-CGRP monoclonal antibodies be combined with onabotulinumtoxinA?

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Background and aims: Chronic migraine (CM) patients constitute 8% of migraine patients. Those on onabotulinumtoxinA (onabotA) with suboptimal response, are left with few therapeutic options. Anti-CGRP monoclonal antibody therapy (mAb) was recently approved, but there is no evidence of the efficacy or safety of combining both medications. We present two cases were dual treatment was used, based on potential synergy.
Results: Clinical cases: 40-year-old woman, with migraine without aura non-responsive to amitriptyline 50mg/day, venlafaxine 225mg/day and candesartan 16mg/day. With a mean of 10,5 headaches/month and high impact on functionality, she started onabotA 155U/trimestral. After an initial improvement, headache frequency worsened without response to increasing dose to 195U. After the sixth treatment, fremanezumab 225mg/monthly was added with substantial improvement. 1-year follow-up she has 3-4 headache days/monthly. 37-year-old man with chronic migraine with aura, mean 20 headaches/month, non-responsive to amitriptyline 75mg/day; flunarizine 10mg/day; topiramate 200mg/day or venlafaxine 75mg/day. He had one period of analgesic overuse, that was well managed. OnabotA 155U/trimestral was then started, and after the first treatment, given his disability, erunumab 140mg/monthly was added, with progressive improvement, reaching a plateau of eight headaches/month.
Conclusion: Good clinical outcome without any adverse reaction was observed in these patients. There is still no literature supporting the benefit of combining onabotA and anti-CGRP mAbs in chronic migraine. They have independent mechanisms of action, good safety profile with no superimposed risk, and, most of all, good outcomes in headache trials. Their combination, may prove beneficial in future studies, especially if other factors for chronicity have already been managed.
Disclosure: Nothing to disclose.

EPO-273

Cluster Headache: what to expect from neuroimaging?

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Background and aims: To describe the neuroimaging findings in 40 patients with cluster headache (CH).
Methods: We reviewed the medical records of patients carrying the diagnosis of CH who attended our hospital for the last 10 years. 32 patients actually had diagnosis criteria for either chronic or episodic CH. We also examined 959 records of migraine patients: eight out of them suffered in fact from CH. Six CH patients showed atypical features. We finally reviewed the neuroimaging findings of 40 CH patients.
Results: Brain MRI was performed in 30 patients: 20 were normal and 10 showed these findings: left MCA/ACA stroke, retrocerebellar cyst, frontal skull haemangioma, chronic ischemia, prominent basilar artery, chronic microbleeding vs brain calcification, maxillary sinusitis, asymmetric lateral ventricles, left frontoparietal necrotic lesion secondary to traumatic brain injury, and left trigeminal schwannoma. Only the latter was considered to be the cause of the headache. This patient had a CH according to IHS criteria but also had paresthesias in left V1-V2 territory. A head CT was performed in seven patients: five were normal and two showed sinusitis. No imaging was available from 3.
Conclusion: We only found one case of atypical CH with a symptom related lesion. In all our cases of typical CH, the neuroimaging was normal or did not show relevant findings. Our sample is insufficient to establish strong recommendations. It would be worthwhile to carry out larger studies to assess the profitability of the test in typical CH, since they may lead to standard clinical practice changes.
Disclosure: No conflict of interest.

EPO-274

Cost offsets for erenumab responders regarding migraine healthcare resource use and productivity loss in Portugal

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Background and aims: Migraine prophylaxis is still an area of large unmet medical needs. Although some patients may benefit from oral standard-of-care treatment options, poor tolerability and low adherence and persistence call for alternative therapies with improved long-term tolerability and safety profiles. Erenumab is the sole fully human monoclonal antibody indicated for migraine prophylaxis in adults who have at least four monthly migraine days (MMD). We aimed to assess the cost offsets of erenumab 140mg in responders (≥50% relative MMD reduction versus baseline) with three or more prophylactic treatments failures (TF3+).
Methods: Changes in migraine-related health resource use (HCRU) and productivity loss in responders were estimated using a published responder analysis tool based on data from clinical trials with erenumab. The societal perspective was taken for the cost analysis. Unitary costs were extracted from Portuguese official sources and were expressed in 2020 euro.
Results: The estimated change of disease burden in erenumab responders is described in Table 1. Based on these changes, we expect cost offsets of 5,557 € per responder treated with erenumab 140mg. Accounting for the erenumab acquisition cost (13 administrations/year), annual savings of 879 € per responder is foreseen. The cost offsets driver is productivity loss (Figure 1).

Health resource use and productivity loss	Before	After	% change
Migraine specific medication (days)/month	8.2	2.3	-69%
Headache medication (days)/month	5.0	2.0	-59%
Hospitalizations/month	0.047	0.040	-16%
Emergency room visits/month	0.108	0.067	-37%
GP visits/month	0.562	0.380	-33%
Nurse visits/month	0.115	0.120	12%
Neurologist visits/month	0.058	0.017	-69%
Absenteeism (hours)/month	18.1	6.5	-60%
Presenteeism (hours)/month	41.3	17.0	-55%

Table 1 - Changes of monthly health resource use and productivity loss in erenumab responders

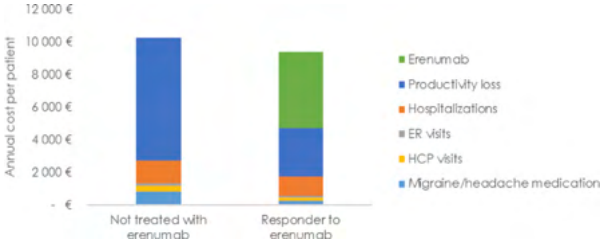

Figure 1 - Estimated annual cost per patient

Conclusion: Erenumab 140 mg brings cost-savings to society in responders (patients who stay on treatment in the mid- and long-term) due to reduced HCRU and work productivity gains. Cost offsets would become even larger if the effect of erenumab in patients' quality of life have been accounted for in this monetary analysis.
Disclosure: Authors are Novartis employees.

EPO-275

Microvascular decompression in morbidly obese and normal weight patients, a comparative analysis

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Background and aims: Trigeminal Neuralgia (TN) is a painful condition associated with deterioration in quality of life. Microvascular decompression (MVD) is considered the procedure of choice due to its high efficacy and safety profile; however, surgeons are reluctant to perform MVD in patients with high degrees of obesity. The aim of the present study is to compare the safety and efcacy of MVD in patients with morbid obesity and normal weight.
Methods: Retrospective analysis of clinical data was performed in patients who underwent MVD from 2017 to 2020 in our clinic. Among 310 operated patients for Classic TN in that period, we included 37 patients with normal weight and 23 grade III obesity. Peri-operative and outcome data from patients were compared in both groups.
Results: Mean of BMI was 22.6 and 43.1 for normal weight and obese patients, respectively. Cost of surgical procedure, rates of preoperative comorbidities and Simplified Airway Risk Index were higher in the obese group. Symptom characteristics, number of medications, hospital stay, short-/long-term complications and pain relief were similar between both groups.
Conclusion: MVD for patients with morbid obesity can be achieved safely with careful perioperative management. Despite a higher prevalence of comorbidities and the difficulty to intubate obese patients, the rate of complications and successful outcomes after MVD were comparable to normal weight patients. MVD should be considered in obese patients when it is the only effective treatment that can improve their quality of life.
Disclosure: The authors have nothing to disclose.

EPO-276

Effect of anandamide on the CamKII and VPAC1 expressions in the nitroglycerin model of migraine

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Background and aims: In migraine, the activation and sensitization of the trigeminal system seems to pivotal during attack and it appears that calcium/calmodulin-dependent protein kinase II alpha (CamKII), pituitary adenylate cyclase-activating polypeptide (PACAP) are involved in its pathogenesis. One of the animal models of migraine uses the systemic administration of nitroglycerin (NTG). The endocannabinoid system is thought to play a modulatory role in the trigeminal system and anandamide (AEA) has been widely examined in this context. In the present experiment, we investigated the effect of NTG and AEA on CamKII and vasoactive intestinal polypeptide type 1 receptor (VPAC1) expression levels in the upper cervical spinal cord of rats.
Methods: The animals were divided into four groups: animals in the first group received vehicle solution as treatment; in the second group, the rats were treated with an intraperitoneal injection of NTG; rats in the third and forth groups received AEA half hour before and one hour after the placebo or treatment with NTG. Four hours after placebo/NTG injection, the animals were perfused and the cervical spinal cords were removed for western blotting.
Results: Our results show that both NTG and AEA alone can increase CamKII and VPAC1 expression in the spinal cord segments. A combination of NTG and AEA has an opposite effect on these markers.
Conclusion: We hypothesized that the combined treatment, which cause a huge boost of nitric oxide (NO) surge will decrease the levels of NO on the long run by a negative feedback mechanism.
Disclosure: Supported by the ÚNKP-20-4 – New National Excellence Program of the Ministry for Innovation and Technology from the source of the National Research, Development and Innovation Fund.

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EPO-277

Outside the box: diagnostic challenges in a globalized world – a myelopathy case study

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Background and aims: Myelopathies represent a varied pathologic group with a broad etiological range including autoimmune, infectious, neoplasic and vascular. The relative incidence and its epidemiological factors are quite variable, strongly influenced by the clinical context. As such, the diagnostic approach may encompass specific diagnostic challenges.
Methods: Case study: A 38 year old male originally from Brazil but living in Portugal for four years was admitted with low back pain, erectile dysfunction, accompanied by weakness and tingling of both lower limbs. Initial neurological assessment also revealed absent reflexes and hypopallestesia bilaterally, increased pinprick along the left L4-S1 territory and ataxic gait. MRI revealed hypersignal in T2 and STIR along the conus medullaris up to C5-C6, with greater oedema and medullar expansion between the conus and T7-T8.
Results: Given the patient's history and imaging, further serological testing for anti-schistosome antibodies was positive, although stool parasitological testing was negative. Corticoid therapy was prescribed with immediate clinical improvement, followed by treatment with Praziquantel. In the following six months the patient had recovered autonomous gait with further improvement noted on MRI.
Conclusion: Although the involvement of the central nervous system is an uncommon complication of Schistosomiasis, the presumptive diagnosis should not be neglected. The extensive medullary involvement seen in this patient is also a rather uncommon feature, since the most typical presentation is usually limited to the conus. Neuro-schistosomiasis by S. Mansoni still represents an important public health problem in many parts of the world. Its clinical manifestations may present late, highlighting the importance of a thorough history taking.
Disclosure: Nothing to declare.

EPO-278

A Computational Model with Quantum Mechanics Methods for Microcephaly and Neuropathophysiology in Zika Virus Infection

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Background and aims: The scientific literature suggests a relationship between Zika virus infection and microcephaly. This study aims to develop a computational model with quantum mechanics methods for microcephaly and neuropathophysiology in Zika virus (ZIKV) infection.
Methods: The model was elaborated based on computational simulations that analyzed (a) ZIKV infection mechanisms; (b) ZIKV genome structure and signaling transductions underlying ZIKV infection; (c) vertical transmission of ZIKV and its impact on human fetal development; (d) investigation of neurotropism of ZIKV infection; (e) mechanisms underlying impaired brain development upon ZIKV infection. The model, computational simulations and analyzes of this scientific work were elaborated with the use of software: ACD/ ChemSketch, Swiss-PdbViewer, ABCpred, BepiPred-2.0, DEseq, GOseq, BiNGO, AxonDeepSeg, Computer-assisted Evaluation of Myelin formation (CEM), PyMol, ICM-Browser, Visual Molecular Dynamics (VMD), C-ImmSim, Simmune and ChemDraw.
Results: Increased levels of IFN--inducible protein 10 (IP-10), interleukin-6 (IL-6), IL-8, vascular endothelial growth factor (VEGF), monocyte chemoattractive protein 1 (MCP-1), and granulocyte colony-stimulating factor (G-CSF) were identified as factors that assist in the process of damage to the central nervous system by Zika virus infection. Neural progenitor cells (NPC) are targets of the Zika virus in the brain inducing dysregulation in the neuroimmune response processes. This work suggests that p53 and caspase inhibitors can efficiently prevent Zika Virus-induced NPC death being an important factor in the process of diagnosis and analysis of the development of microcephaly.
Conclusion: Understanding pathological mechanisms should help developing therapeutic tools to treat, diagnose and analyze the microcephaly.
Disclosure: Nothing to disclose.

EPO-279

Leptomeningeal dissemination of glioblastoma mimicking gummatous syphilis and tabes dorsalis: a case report

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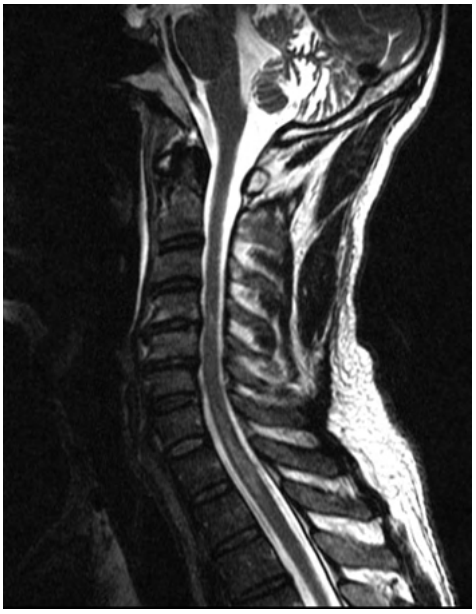
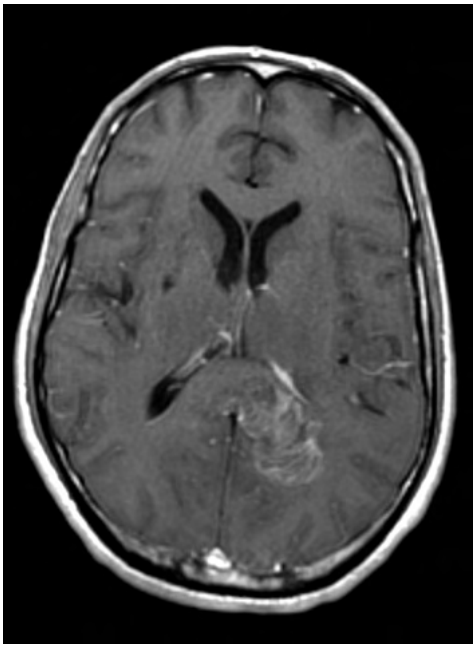
Background and aims: Neurosyphilis can manifest through various neurological syndromes, classically divided into early and late forms. Syphilitic gummas are granulomatous processes, observed in advanced stages, often mistaken for space occupying lesions.

Methods: Case report

Results: A 52-year-old male with a 10-year history of gait ataxia was admitted with worsening of gait instability, memory and behavioral changes. Medical history included smoking, alcohol consumption and syphilis, diagnosed 15 years prior, with uncertain adherence to treatment. Examination showed mild cognitive impairment, slow smooth pursuit movements, right peripheral facial palsy, right hemiparesis, truncal and appendicular ataxia and proprioceptive errors in the lower limbs. MRI revealed T2-hyperintense lesions in the left pons, middle cerebellar peduncle, cerebellar cortex and an expansive lesion near the atrium of the lateral ventricle infiltrating the contralateral white matter through the corpus callosum; enhancement of the V, VII and VIII cranial nerves on post-gadolinium T1-weighted sequences and a longitudinal posterior intramedullary lesion. He had elevated CSF proteins and white blood cells with positive treponemal (TPHA) and non-treponemal (VDRL) tests in both blood and CSF. CSFcytology and flow cytometry were unremarkable. He was started on IV penicillin and later on corticosteroids. His clinical status progressively deteriorated leading to death. Autopsy revealed a glioblastoma with extensive leptomeningeal dissemination.



Sagittal T2-weighted MRI of the spinal cord.



Axial T1-weighted post-contrast brain MRI.

Conclusion: Syphilis is often referred to as "the great masquerader" as it may resemble a variety of diseases. We describe an unusual presentation of glioblastoma with cranial nerve invasion and spinal cord involvement, mimicking gummatous syphilis and tabes dorsalis, in a patient with diagnostic criteria for late neurosyphilis.

Disclosure: No disclosures.

EPO-280

Neurosyphilis presenting with brainstem ischemic stroke

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Background and aims: Syphilis is a sexually transmitted infection caused by Treponema pallidum that may present with neurological symptoms, usually mild.
Methods: Case-Report
Results: A 41-year-old male, smoker, otherwise healthy, presented to the Emergency Department 12 hours after last known well, with complaints of dysarthria, left hemi weakness and right hemi hypoesthesia scoring seven in the National Institute of Health Stroke Scale (NIHSS). Brain CT and CT-Angiography were performed, demonstrating an acute left paramedian pontine infarction, without large vessel occlusion. No reperfusion therapy was instituted. The patient was admitted to the stroke unit where his clinical status worsened with right hemiplegia and increased respiratory effort, scoring 22 in NIHSS and requiring intubation. An MRI with angiography was performed confirming a brainstem and cerebellar infarction, associated with several vascular irregularities and severe stenosis/occlusion in both posterior and anterior circulation. Cardiovascular, autoimmune and prothrombotic studies were normal. HIV and syphilis screening were positive, with reactive TPPA and VDRL titters of 1:32 and CD4 cell count >200/mm^3. A lumbar puncture was performed, showing pleocytosis with normal glycorrhachia and a reactive VDRL; microbiology culture tests, PCR for Toxoplasma gondii, Mycobacterium tuberculosis, Varicella zoster, Epstein-Barr, Cytomegalovirus, HIV, Listeria were negative. The patient was treated with penicillin, a 5-day course of methylprednisolone due to the exuberant vasculitic component and started antiretroviral therapy and rehabilitation, with marked improvement.
Conclusion: This is an atypical case of a massive ischemic stroke due to meningovascular neurosyphilis. It highlights the importance of syphilis as a cause of stroke, particularly in young patients.
Disclosure: Nothing to disclose.

EPO-281

Neurological manifestations in patients with COVID-19: a Tunisian study

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Background and aims: Various neurological manifestations have been reported in association with the coronavirus disease of 2019 (COVID-19) and may be the initial or only presentations of the disease. Even, the virus increased risk of exacerbations of chronic neurological disorders.
Methods: We conducted a prospective study in the department of neurology of the Military Hospital of Tunis from September 2020 to December 2020 including patients hospitalized for COVID-19 with neurological manifestations. The diagnosis was made by real-time reverse-transcription polymerase chain reaction (RT-PCR) analysis of nasal swab specimens.
Results: 14 patients were included. Cerebrovascular complications of COVID-19 were: acute ischemic stroke (n=5), cerebral hemorrhage (n=1) and cerebral venous thrombosis of the sigmoid sinus (n=1). Two patients with previously stable myasthenia gravis had myasthenic exacerbation and one of them required intubation for hypoxemic respiratory failure. Decompensation of chronic neuroinflammatory disorders was observed in two cases: relapse of multiple sclerosis (n=1) and Neuro-Behçet's disease (n=1). One patient followed for epilepsy was hospitalized for uncontrolled seizure following infection with COVID-19, and two patients had clinical findings of encephalitis including confusion, headache and fever. The outcome was favorable for 12 patients who received symptomatic treatment of COVID-19 along with treatment for their disease. Two patients with ischemic stroke were died.
Conclusion: In the current pandemic context, physicians should be aware of the broad spectrum of neurological signs of COVID-19 for early diagnosis and management of patients.
Disclosure: Nothing to disclose.

EPO-282

A study of pattern of distribution of various GBS variants across Central-South India

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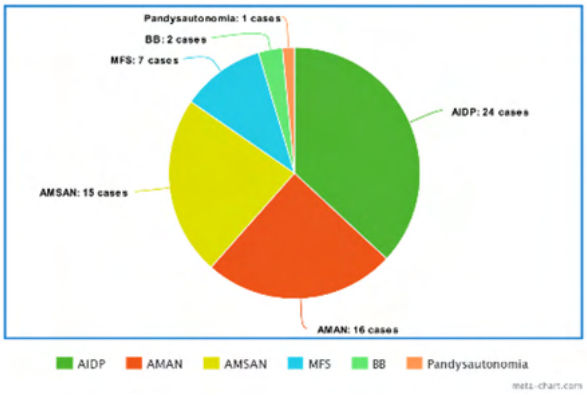
Background and aims: Guillain Barre Syndrome (GBS) is an acute infective neuropathy which is classically characterised by ascending motor weakness, areflexia and albumino-cytological dissociation in CSF. Although it is commonly seen in this form, there are many variants of GBS which have been continuously described in the literature and have got varied clinical as well as investigatory pattern. This study was done to observe the pattern of prevalence and distribution of GBS and it's variants across Central-South regions of India.
Methods: This was a retrospective observational study done over three tertiary referral centres from Central and South India over a period of two years from 1st January 2019 to 31st December 2020. All the cases diagnosed to be any of the GBS variants were included in the study. The pattern of distribution was observed.
Results: A total of 65 cases of GBS were seen. Acute Inflammatory Demyelinating Polyradiculoneuropathy (AIDP) was the most common form seen in 24 cases. It was followed by 16 cases of Acute Motor Axonal Neuropathy (AMAN) and 15 cases of Acute Motor Sensory Axonal Neuropathy (AMSAN). Seven patients of Miller Fisher Syndrome(MFS) were seen. Two patients were diagnosed to have Bickerstaff Brainstem(BB) encephalitis and one patient had pandysautonomia variant.



Distribution of variants

Conclusion: There are many variants of GBS out of which AIDP is the commonest form. Proper history, examination and meticulous investigatory approach is needed to identify the various manifestations of the spectrum of GBS.
Disclosure: Nothing to disclose.

EPO-283

Bilateral internuclear ophthalmoplegia associated with SARS-COV2 infection

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Background and aims: Internuclear ophthalmoplegia (INO) can be caused by a multitude of mechanisms leading to lesion of the medial longitudinal fasciculus (MLF), including infection. Currently, neurological manifestations have been described in COVID-19 patients, either due to immune mediated response or direct viral invasion of the central nervous system.
Methods: Report of a clinical case
Results: A previously healthy 54-year-old male presented with complaints of sudden onset dizziness and diplopia, preceded by self-limited diarrhea the day before. At examination the patient was apyretic. Neurological examination was striking for a hypertrophic right eye and a bilateral INO, but was otherwise unremarkable. Brain computed tomography scan with contrast was normal, as well as standard blood tests. RT-PCR for SARS-Cov2 was negative, as tests for HIV, VDRL, hepatitis A, B and C viruses, CMV, Borrelia, botulism and IGRA test. Stool microbiologic study was negative. Brain MRI and CSF studies were normal. Autoimmunity panel tests, including acetylcholine receptor antibody, anti-MuSK, anti-GQ1b and onconeural antibodies, were within normal range. A 5-day course of high-dose intravenous methylprednisolone was started, with progressive symptoms improvement and resolution of diplopia. One week after discharge, a serologic COVID-19 test was requested, which was positive for IgG and IgM, with a negative RT-PCR test.
Conclusion: In this case, despite the lack of imaging findings, namely in the brainstem, the dramatic clinical response to anti-inflammatory therapy seems to favor an immune mediated mechanism. After extensive negative workup, the serologic positive test suggests a potential relationship between a bilateral INO and SARS-Cov2 infection.
Disclosure: The authors have nothing to disclose.

EPO-284

Cauda equina syndrome caused by cytomegalovirus infection (Elsberg syndrome) in an immunocompetent patient

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Background and aims: Cauda equina syndrome (CES) is an uncommon but potentially urgent condition. Time from symptom onset to starting treatment may be associated with prognosis. Acute or subacute bilateral lumbosacral radiculitis, with or without myelitis in the lower spinal cord, referred to as Elsberg syndrome, is an infrequent CES etiology, caused by human herpesviruses and mostly affecting immunocompromised individuals. Functional recovery is usually poor.
Methods: A 23-year-old male without relevant prior history was admitted for weakness in the lower limbs, paresthesia in the soles of the feet, difficulty in contracting the sphincters and erectile dysfunction, evolving over one week. Neurological examination upon arrival found moderate symmetric weakness in knee flexion and dorsiflexion and plantar flexion of the feet, saddle hypoesthesia and absent lower limb reflexes with plantar flexor responses.
Results: Magnetic resonance showed diffuse enhancement of the cauda equina roots (Figure 1). Analysis of the cerebrospinal fluid revealed mononuclear pleocytosis with normal glucose. Serology revealed positivity for cytomegalovirus IgM and IgG, the rest (including human immunodeficiency virus) being negative. Treatment with acyclovir, already started empirically, was maintained for two weeks and one gram of methylprednisolone was administered for five days. At discharge, two weeks after diagnosis, the patient was able to walk on his toes and heels, he did not present hypoesthesia or paresthesia, and the sphincter and erectile functions had normalized.

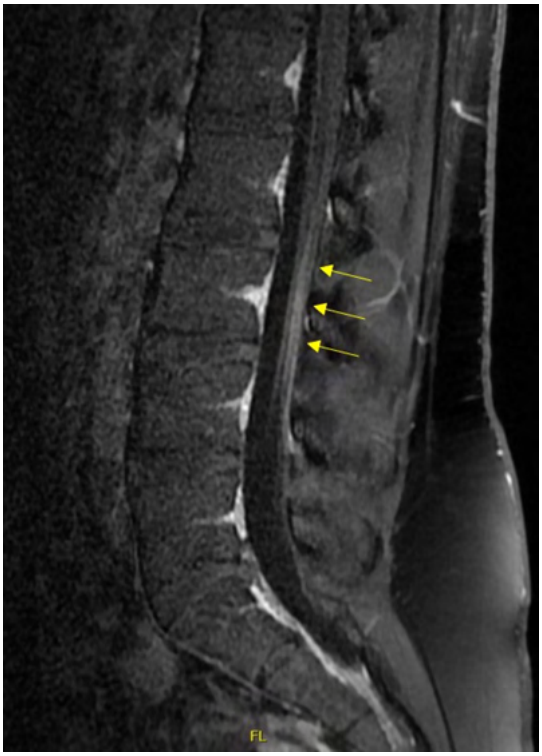

Figure 1. Sagittal plane of contrast-enhanced T1-weighted MRI showing diffuse linear enhancement of the cauda equina roots.

Conclusion: Infections in general and cytomegalovirus in particular are a rare etiology of CES. An early diagnosis can lead to promptly consider specific treatment to prevent irreversible neurological damage.
Disclosure: Nothing to disclose.

EPO-285

Epstein-Barr virus meningoencephalitis in an elderly patient: clinical presentation, diagnostic workup and outcome

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Background and aims: Epstein-Barr virus (EBV) infection can generate several clinical forms of central nervous system (CNS) involvement. Meningoencephalitis presentation is relatively rare and occurs almost exclusively due to the reactivation of latent virus in the setting of severe immunosuppression.
Methods: We present the case of a 78-year-old female admitted for constitutional syndrome, postprandial vomiting, vertical diplopia and gait instability, evolving over two months. She had no relevant prior history. Neurological examination upon arrival found skew deviation with vertical diplopia in primary position and left gaze, a pathological gaze-evoked nystagmus and moderate gait ataxia.
Results: Magnetic resonance imaging (MRI) showed patchy areas of signal alteration of the supra and infratentorial parenchyma with vascular and leptomeningeal enhancement (Figure 1). Analysis of the cerebrospinal fluid (CSF) revealed predominantly mononuclear pleocytosis along with a persistently positive EBV PCR and high EBV load (6.88 10^3 DNA copies/ml). Brain biopsy showed nonspecific findings, without data suggestive of neoplastic or inflammatory involvement. Human immunodeficiency virus testing was negative, and no cause of immunosuppression was found in the rest of the studies performed. Acyclovir was administered for 14 days, leading to a progressive clinical improvement. The patient was able to walk unaided and vomiting had disappeared at discharge. Only a mild diplopia persisted.

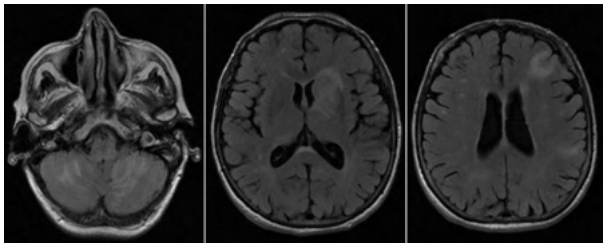

Figure 1. MRI FLAIR sequence showing hyperintensity foci in the cerebellum, left basal ganglia and subcortical zone of the left frontal and parietal lobes.

Conclusion: EBV meningoencephalitis should be included in the differential diagnosis of multifocal CNS involvement. MRI and CSF are essential for diagnosis. Brain biopsy can be considered if etiology is still unknown. Time from symptom onset to starting treatment may be associated with prognosis. Therefore, high diagnostic awareness is necessary.
Disclosure: Nothing to disclose.

EPO-286

Atypical Ramsay Hunt Syndrome

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Background and aims: Ramsay Hunt syndrome (RHS)is characterized by acute facial palsy often unilateral with herpetic eruption on the auricle ans external ear canal. This syndrome was attributed to infection by Varicella Zoster Virus (VZV), which becomes latent in sensory ganglia after primary infection and emerges from latency to cause zoster. Some atypical presentation can however be seen.
Methods: Describe the clinical, paraclinical and therapeutic aspects of a patient with atypical RHS
Results: A 65-year-old woman with a history of arterial hypertension, arrived to our emergency room with bilateral facial muscular deficits and bilateral facial hypoesthesia and onset of hearing loss since two days. The clinical examination revealed bilateral facial paralysis and bilateral involvement of the trigeminal and vestibulocochlear nerve. MRI documented bilateral contrast enhancement of the VII and V nerve. Lumbar puncture showed hyperproteinorachia with 11 white elements with negative neoplastic cells. Biological investigation (tumor markers, conversion enzyme level, infectious serologies for Brucella and lyme) were negative. Anti VZV IgG Antibody were strongly positive at 1,263mIU/ml with negative IgM. The diagnosis of RHS was retained and the patient was treated with acyclovir and systemic steroids with marked improvement.
Conclusion: Atypical form of RHSwith absence of vesicular rash and bilateral peripheral paralysis that may appear as one of the symptoms of a system disease, can mislead the diagnosis. High levels of antibody titer of anti VZV or cochleo vestibular signs can help the diagnosis. Early treatment on RHS with systemic steroids and acyclovir is crucial for recovery.
Disclosure: Nothing to disclose.

EPO-287

Effectiveness of the complex therapy of neurological syndromes in HIV infection

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Background and aims: The aim of the study was to optimization of pathogenetically based approach to complex therapy of major neurological syndromes in HIV patients.
Methods: The study is based on the survey data of 103 patients with HIV infection (54.4% of women and 45.6% of men), aged from 20 to 45 years. Neuropsychological studies were carried out using special tests, such as, Wechsler Memory Scale (WMS), "Schulte tables" and "Incomplete contours of objects" (AR Luria). The efficacy of citicoline (1,000mg/day) when added to basic HIV therapy was studied in 53 patients. The comparison group consisted of 50 HIV patients who did not receive neuroprotective therapy.
Results: In the main group, against the background of the therapy with the inclusion of ceraxon, no deterioration was noted. In the course of the observation dynamics, there was an improvement in memory indices, characterized by a significant increase in the mean equivalent memory indices (EMI) (96.8±2.5 versus 112.6±3.8; $p<0.05$). In the comparison group, there is also a tendency to an increase in the average EMI values. 46.7% patients in main group showed expressed improvement, and 53.3% had a moderate improvement. An expressed improvement in patients from the comparison group was in 32.0% patients, moderate was in 48.0%. In 12.0% of patients, there was a minimal improvement in their condition, and in 8% there was no improvement.
Conclusion: The present study has demonstrated the effectiveness of citicoline (ceraxone) in the treatment of neurological disorders in patients with HIV.
Disclosure: Nothing to disclose.

Movement disorders 1

EPO-288

Drooling in Parkinson's Disease

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Background and aims: Sialorrhea is drooling or excessive salivation from the corners of the mouth is apparent in approximately 75% of individuals with PD and was historically interpreted as resulting from hypersecretion of saliva because of autonomic dysfunction. Alteration in salivary gland function is believed to arise from PD-associated changes in the autonomic nervous system and possibly involves the salivary para-sympathetic ganglia. Irrespective of the amount of saliva produced, drooling probably occurs because of a PD-related inability to efficiently swallow with normal frequency, an inability to fully close the mouth, and an anterior flexed head position.
Methods: In this retrospective study we investigated the prevalence of drooling in 106 PD patients, 62 or 58.5 % males and 44 or 41.5 % females. In addition we studied the impact of gender on drooling in this patient population.
Results: Our results show that a significant correlation exists between drooling and stages of disease in our sample of PD patients. Furthermore, in males, the correlation between the prevalence of drooling was found to be clinically significant as compared to the female population.
Conclusion: Our findings suggest that drooling is a major concern in the course of PD and should addressed and treated early in patients with PD.
Disclosure: Nothing to disclose.

EPO-289

Potential drug-drug interactions in patients with Parkinson's disease identified by Epocrates and Medscape

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Background and aims: Levodopa, of the mainstay of Parkinson's disease (PD) therapy, is frequently interacting with numerous drugs. The aim of this study was to identify predictors of potential drug-drug interactions (pDDIs) in PD patients.
Methods: This was a retrospective cross-sectional study in PD patients at the Clinic of Neurology, Clinical Center Kragujevac, Serbia. Medical records of hospitalized patients during the period 2017–2019 were reviewed. The pDDIs were identified by parallel use of two relevant, free-available relevant interaction checker databases- Epocrates and Medscape. Multivariate regression methods were used to reveal potential predictors of number of pDDIs per patient.
Results: Epocrates detected 295 different pDDIs in 97.2% of 72 patients with PD. The most frequent pDDIs were those that involved levodopa (with bisoprolol and clonazepam). Predictor of pDDIs in general was total number of drugs and use of antidepressants. Medscape revealed 289 different pDDIs in 97.2% of patients. The most common pDDIs were levodopa-bisoprolol and acetylsalicylic acid-bisoprolol. Total number of drugs and number of diagnosis were identified as the relevant predictors of pDDIs.
Conclusion: The main predictors of pDDIs in PD patients were total number of drugs, number of diagnosis and therapy with antidepressants. Therefore, clinicians should pay particular attention to the posibility of pDDIs in PD patients who are treated with antidepressants, as the most frequently prescribed therapy for non-motor symptoms of PD.
Disclosure: Nothing to disclose.

EPO-290

Prospects for the use of audio-visual stimulation in the treatment of some non-motor symptoms of Parkinson's disease

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Background and aims: Today, there is no effective pharmacological treatment for many nonmotor PD symptoms. Audio-visual stimulation (AVS) is non-invasive neuromodulation techniques, the action of which is able to modify the thalamocortical loops. Moreover, AVS action through the retina-hypothalamic tract may have an effect on the PD symptoms associated with the day/night cycle.
Objective: To evaluate the AVS effectiveness on sleep disorders, depression level and visual hallucinations (VH) in PD patients.
Methods: 23 PD patients with VH aged 47–65 years and 20 healthy people were examined using polysomnography (PS). The AVS duration was 25 minutes for 14 days. The following tests were used twice (on the first and last day of AVS application): Parkinson`s Disease Sleep Scale (PDSS-2), RBD-Screening Questionnaire, Epworth Sleepiness Scale (ESS), Beck Depression Inventory.
Results: PS analysis revealed a decrease in total sleep time, prolongation in sleep latency and increased amount of REM sleep in PD patients (table 1). We found significant improvement in the subjective and objective sleep, depression level reduction, as well as a decrease in the VH duration after AVS (table 2).

Variables	PD patients n =23	Control group n =20
	Me (Q1, Q3)	
Age	58 (50; 61)	56 (50; 59)
PD duration (years)	7 (5; 9)	-
UPDRS (part I)	20 (16; 25)	-
UPDRS (part III)	38 (28; 52)	-
MMSE	23 (18; 26)	29 (29; 30)
Polysomnography		
Total sleep time (hour)	268 (187; 345)	323 (266; 435) *
Sleep onset latency (min)	33 (5; 61)	18 (10; 36) *
REM episodes	2 (1; 4)	3 (1; 4)
REM sleep duration (min)	70 (49; 81)	54 (42; 66) *

MMSE: Mini- Mental Status Examination
Me (Q1, Q3) - Median (lower and upper quartiles)
** - Statistically significant difference (p < 0.05) in Mann-Whitney U test*

Table 1. Comparative characteristics of PD patients and control groups

Variables	Before AVS application	After AVS application
	Me (Q1, Q3)	
PDSS-2	23 (18; 29)	16 (13; 24)*
RBD-Screening Questionnaire	7 (4; 10)	5 (3; 8)*
ESS	12 (5; 16)	11 (4; 14)
Beck Depression Inventory	19 (12; 31)	13 (10; 22)*
Hallucinations, (simple/complex), n	14/6	11/2
• Frequency (per week)	3 (1; 6)	2 (0; 4)
• Duration (minutes)	5 (1; 30)	2 (0; 15)*
Polysomnography		
Total sleep time (hour)	268 (187; 345)	295 (214; 381) *
Sleep onset latency (min)	33 (5; 61)	26 (18; 45) *
REM episodes	2 (1; 4)	3 (1; 4)
REM sleep duration (min)	70 (49; 81)	59 (40; 68) *

Me (Q1, Q3) - Median (lower and upper quartiles)
** - Statistically significant difference (p < 0.05) in the Wilcoxon Matched Pairs Test*

Table 2. Comparative assessment of testing and polysomnography data before and after the AVS course

Conclusion: Changing the activity of many brain structures via neural pathways to the thalamus where audio and visual sensory information is processed, AVS can be successfully used in the treatment of depression, sleep disorders and specific conditions, such as REM sleep behavior disorder in PD patients. AVS is also seen as a promising treatment for VH, including those caused by anti-parkinsonian medications.
Disclosure: Nothing to disclose.

EPO-291

Automated mechanical peripheral stimulation effects on gait impairment in Parkinson Disease

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Background and aims: Gait impairment, especially freezing of gait in Parkison Disease (PD) is a major contributor to decreased quality of life. This study aims to evaluate the change in gait parameters in subjects with PD before and after Automated Mechanical Peripheral Stimulation (AMPS) treatment.
Methods: Six subjects with PD and gait impairment (3 females and three males, mean age 76 years, Hoehn and Yahr Scale 3, disease duration 5.6 years) participated in this study. A dedicated medical device (Gondola Medical Technologies, Switzerland) was used to administer a single AMPS therapy. All patients were treated in off levodopa phase, using active and placebo treatment. They were evaluated with Timed Up and Go (TUG) test and 10 meter walk test (10 MWT). For the statistical analyses, non-parametric Wilcoxon ranked test was applied to assess the intervention effects.
Results: A Wilcoxon signed-rank test showed that the AMPS treatment elicited a significant improvement in TUG test (Z=-1.992, p=0.046). On the other hand, the AMPS treatment did not elicit a significant improvement in 10MWT speed (Z=-1.363, p=0.173), nor the number of steps (Z=-0.318, p=0.750). Two patients experienced a maintained significant clinical improvement, especially of freezing of gait for at least four days. The study is limited by the small sample number of participants.
Conclusion: The result of this study may give new insights on the AMPS as an effective adjunct therapy for the improvement of gait performance in patients with PD, although further studies are required.
Disclosure: The authors declare that they have no competing interest.

EPO-292

The Impact of Non-Motor Symptoms on the Quality of Life of Parkinson's disease patients

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Background and aims: Parkinson's disease (PD) is a neurodegenerative disease characterized by traditional motor features. However, non-motor symptoms (NMS), which inevitably emerge through the disease progression, are common amongst and are often under-recognized and untargeted. The aim of this study is to investigate the impact of non-motor symptoms on quality of life in patient with Parkinson's disease.
Methods: 87 PD patients were prospectively recruited between 2017 and 2020. Multiple methods were used to evaluate the impact of non-motor symptoms (as assessed by the NMS Scale [NMSS]) on PD patients health-related quality of life (HRQoL) rated by the Arabic version of PDQ-39, taking into consideration the other parameters, in particular age, sex, mood (Beck Depression Inventory), disability (Schwab&England Activities of Daily Living Scale), and PD-specific motor dysfunction (ON-state Hoehn&Yahr/UPDRS).
Results: The mean age was 68 years (42–87) and 56% were female. 77.01% patients were on treatment. Fatigue (81.6%) and mood/cognitive disturbances (78,16%) were the most frequently and severely affected NMSs domains. Other common NMS included urinary (72.41%), memory/attention (70.11%), gastrointestinal (67.81%), and cardiovascular problems (59.77%). All off patients have deterioration in different dimentions of HRQoL, particulary emotional well-being (93.10%), mobility (97.70%) and activities of daily living (95.40%). The PDQ-39 summury index was significantly related to the NMSS total score who was correlated positively with UPDRS I-II-III scores, motor severity evaluated by the UPDRS III(Off and On states), and depression(BDI scores).
Conclusion: In addition to motor disabilities, the burden of NMS impact significantly the quality of life of PD patients. Understanding the pattern and effect of NMS remains very important for better therapeutic management.
Disclosure: Nothing to disclose.

EPO-293

Patterns of olfactory dysfunctions in patients with Parkinson´s disease

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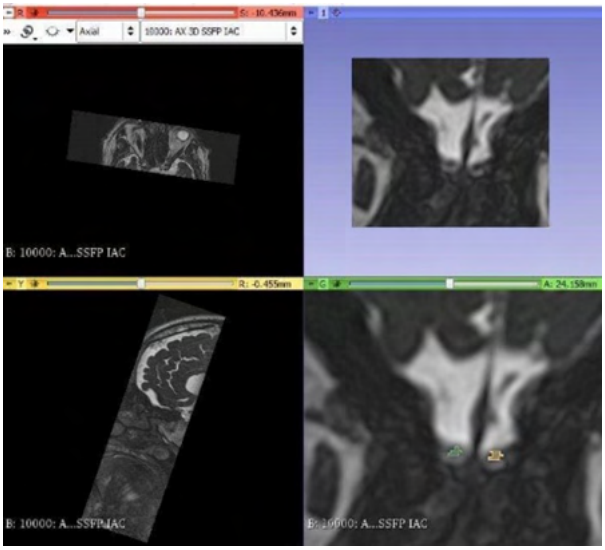
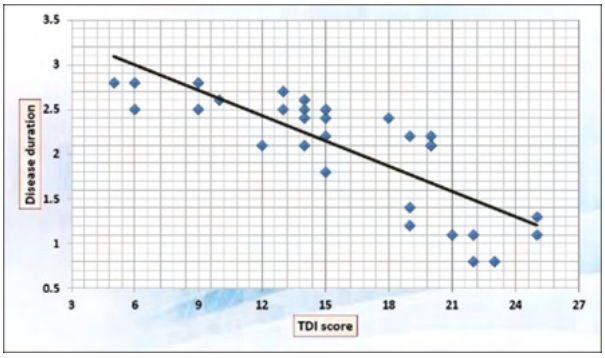
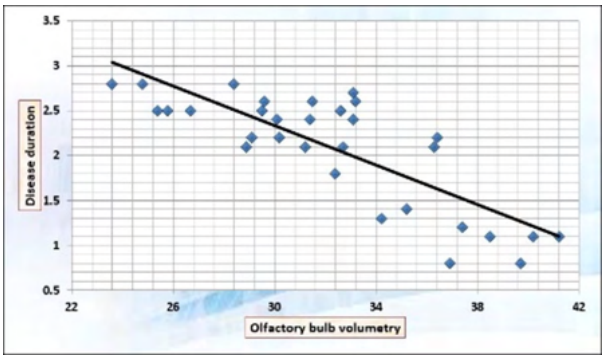
Background and aims: Olfactory dysfunction (OD) is a well-established nonmotor manifestation (NMM) of Parkinson's disease (PD) which needs objective assessment for a better understanding of the disease pathogenesis. The aim of this work was the quantitative and qualitative assessment of olfactory performance in newly diagnosed PD patients.

Methods: This study was performed on 32 recently diagnosed PD patients and 24 healthy controls subjects (HCS) submitted to Unified Parkinson's Disease Rating Scale-III (UPDRS–III), extended n-butanol Sniffin' Sticks test (SST), and olfactory bulbs volumetry (OBV).

Results: There were significant decreases in SST threshold, discrimination, identification, and TDI variables as well as OBV in PD patients compared to HCS. The olfactory performance was negatively correlated with disease duration but had no relation with PD severity as well as a motor subtype.







Conclusion: OD is highly prevalent during the early stages of PD which is both measurable and specific with identification and discrimination impairments to certain odors which makes smell performance testing an important step in PD patients' evaluation.

Disclosure: Nothing to disclose.

EPO-294

Blood lysosomal activities in Parkinson's disease associated with mutations in the GBA gene

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Background and aims: GBA mutations are the most common genetic risk factor for Parkinson's disease (PD). The important role of lysosomal dysfunction in PD associated with GBA mutations (GBA-PD) pathogenesis of was shown. The aim was to determine more insight into changes in lysosomal activity in GBA-PD pathogenesis.
Methods: 12 GBA-PD patients, 16 asymptomatic GBA mutations carriers (GBA-Carriers), 132 PD patients and 135 controls were recruited. GBA, GLA, SMPD1 expressions were analyzed by real-time PCR in CD45+ blood cells. Enzyme activities (GCase, GLA, ASM) and theirs substrates concentration (HexSph, LysoGb3, LysoSM) were measured by LC-MS/MS in dry blood spots.
Results: There was no differences in GBA expression between all groups ($p>0.05$). GCase activity was decreased in GBA-PD and GBA-Carriers compared to PD ($p<0.001$) and controls ($p<0.01$) with increase of HexSph concentration GBA-PD and GBA-Carriers than in PD ($p<0.001$) and controls ($p<0.05$). SMPD1 expression was decreased in PD compared to controls ($p=0.004$). ASM activity was decreased in PD compared to GBA-PD and GBA-Carriers ($p<0.001$) with elevated LysoSM level in PD than in GBA-PD ($p<0.0001$). ASM activity was increased in GBA-Carriers compared to controls ($p<0.001$) with increase of LysoSM in GBA-Carriers compared to GBA-PD ($p<0.05$) and controls ($p<0.0001$). GLA activity was decreased in PD than in GBA-PD ($p=0.04$) with no differences in GLA expression and LysoSM concentration between all groups ($p>0.05$).
Conclusion: GBA mutation carriers are characterized by alteration not only of HexSph concentration and GCase activity but also altered gene expression of other lysosomal enzymes, theirs activities and substrate concentration and it is independent of PD status.
Disclosure: The study was supported by the Russian Science Foundation grant No. 19-15-00315.

EPO-295

Qalb as a biomarker of Parkinson's disease progression

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Background and aims: Detection of biomarkers of various Parkinson's disease (PD) subtypes that differ in the rate of disease progression will allow us to predict intensity of the disease progression, personalize the therapy. Nowadays there is an evidence of involvement of neuroinflammation mechanisms in the pathogenesis of PD. The functional state of the blood-brain (BBB) and the blood–cerebrospinal fluid (BCSFB) barriers in patients with different rates of PD progression is unknown. The ratio of serum albumin to CSF (Qalb) is an indicator of BBB/BCSFB permeability. Objective. Evaluation Qalb values in patients with rapidly progressive and slowly progressive forms of PD.
Methods: The study group (SG) consisted of 31 patients with PD. 11 patients had a rapidly progressive form with a change of the stages up to four years. 20 patients had a slowly progressive form. The control group (CG) included 11 healthy patients. For determination of microalbumin in CSF an immunoturbodimetric method was used. Serum albumin was determined spectrophotometrically. Qalb was calculated as the ratio of serum albumin level to CSF albumin level.
Results: Qalb in SG amounted to 105 [48; 126], compared with CG – 129 [106.5; 194.5], (=0.09). In patients with the rapidly progressive form Qalb was 48 [43; 68] and with the slowly progressive form – 116 [103.5; 190.5]. The differences between the three groups were statistically significant.
Conclusion: The achieved results indicates the role of BCSFB dysfunction in rapidly progressive form of PD, as well as the heterogeneity of PD according to the development mechanisms.
Disclosure: The research was supported by the Ministry of Health of the Republic of Belarus (grant #20190441).

EPO-296

Evaluation of the efficacy, safety and tolerability of the apomorphine infusion pump in the elderly

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Background and aims: Continuous infusion by subcutaneous apomorphine pump is effective in patients with advanced Parkinson's disease. Its use is not recommended if the patient presents dementia or neuropsychiatric symptoms . We evaluated the efficacy, tolerability and safety of subcutaneous apomorphine infusion in elderly patients with advanced Parkinson's disease.
Methods: Retrospective, observational study. 15 patients from our database over the age of 75 who are currently or had been on subcutaneous apomorphine pump therapy. We recorded: time of disease , cognitive assessment, dose and hours per day of infusion, side effects, patient improvement, quality of life, overall impression of caregiver, and reason for withdrawal of treatment.
Results: Six patients were male and nine were female, with a mean age at initiation of treatment of 79.5 years and a measure of years of Parkinson's disease progression of 7.8 years. The most frequent comorbidity was high blood pressure, seven patients had mild cognitive impairment and none had a history of behavioral disturbance, hallucinations, or confusional syndrome. The most frequent side effect was hypotension in seven patients , followed by drowsiness in four patients and confusional syndrome in 3. Eight patients maintained their treatment for more than a year, three maintained it between six months and a year and four withdrew it before six months. The most frequent reason for withdrawal was lack of efficacy due to disease progression. Six of those who maintained the therapy for more than one year lived at home
Conclusion: Subcutaneous apomorphine infusion therapy it is effective and safe for older patients
Disclosure: Nothing to disclose.

EPO-297

Impact of 3-month early versus postponed initiation of opicapone vs entacapone in Parkinson's levodopa-treated patients

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Background and aims: Opicapone (OPC) proved to be effective in treating end-of-dose motor fluctuations in Parkinson's Disease (PD) patients [1,2].
Methods: OPC 50mg and entacapone (ENT) data from BIPARK-I [1] was analysed. Primary efficacy endpoint was change from baseline in absolute OFF-time. Secondary efficacy outcomes included ON-time without-dyskinesia, Unified-PD-Rating-Scale (UPDRS) part-II and III. Patients on levodopa/dopa-decarboxylase inhibitor (DDCi) were randomized to OPC 50mg ('early-start': OPC 50mg-OPC) or ENT ('postponed-start':ENT-OPC) for a 3-month double-blind phase, after which all patients received open-label levodopa/DDCi and OPC for up to 1-year. This post-hoc analysis evaluated the impact of 3-month earlier versus postponed initiation of OPC 50mg by comparing 3-month initial treatment with both OPC 50mg and ENT and a 3-month switch cut-off under open-label OPC treatment.
Results: In total, 198 patients switched from OPC 50mg (n=98) or ENT (n=100) to 1-year OPC open-label extension. At 3-month double-blind endpoint, OPC 50mg showed greater reduction in OFF-time, UPDRS-II and III, and ON-time without-dyskinesia increase. At 3-month open-label cut-off, OPC 50mg-OPC 'early-start' showed greater reduction in OFF-time, UPDRS-III, and ON-time without-dyskinesia increase. Furthermore, at 1-year open-label endpoint, except for UPDRS part II, a statistically significant benefit for ENT-OPC postponed initiation (even as short as 3-months) was still observed. Both OPC 50mg and ENT groups were well tolerated.

Table 1. Baseline characteristics (Safety Set)

Characteristic	DB ENT/OL OPC N=100	DB OPC 50mg/OL OPC N=98
At double-blind baseline		
Male gender, n (%)	64 (64.0)	61 (62.2)
Age, mean years	63.2	63.3
Disease duration, mean years	7.6	7.4
Daily OFF-time, mean hours	6.4	6.2
At open-label baseline		
Daily OFF-time, mean hours	4.9	4.3
Presence of dyskinesia* – yes, n (%)	43 (43.0)	41 (41.8)
Daily levodopa dose, mean mg	606.0	675.2

*From Unified Parkinson's Disease Rating Scale IV item-32
DB, double-blind; ENT, entacapone; OL, open-label; OPC, opicapone

Table 2. Change from double-blind baseline to 3-month open-label, by previous double-blind treatment, including change from open-label baseline to 1-year switch (FAS)

Visit	Statistic	DB ENT / OL OPC (N=100)				DB OPC 50mg / OL OPC (N=98)			
		OFF-time	ON-time without	UPDRS II	UPDRS III	OFF-time	ON-time without	UPDRS II	UPDRS III
DB Baseline	n	100	100	100	100	98	98	98	98
	Mean	386.1	558.9	8.3	26.1	372.0	575.6	8.4	26.0
	SD	113.01	135.09	5.01	13.01	106.87	115.87	5.06	13.28
1-Week DB	n	100	100	-	-	98	98	-	-
	Mean	92.0	47.0	-	-	90.2	71.9	-	-
	SD	125.39	130.26	-	-	120.90	109.87	-	-
*1-Month DB	n	96	96	96	96	98	98	98	98
	Mean	-48.5	95.8	-1.6	-4.5	-133.1	131.7	-1.3	-4.6
	SD	146.74	136.07	3.34	7.64	135.22	129.30	2.99	6.34
*3-Month DB	n	100	100	100	100	98	98	98	98
	Mean	-92.2	94.1	-1.7	-4.7	-112.9	113.9	-1.8	-5.6
	SD	155.76	142.56	3.55	9.00	136.71	127.54	2.72	7.17
1-Week OL	n	100	100	98	98	98	98	98	98
	Mean	-130.2	110.9	-2.1	-5.4	-126.3	124.6	-1.7	-6.0
	SD	170.01	150.37	3.73	8.83	134.15	124.74	2.51	7.44
*1 Month OL	n	97	97	98	98	97	97	97	97
	Mean	-129.2	134.9	-2.5	-5.9	-140.1	140.9	-1.7	-6.7
	SD	159.73	145.98	3.79	8.96	144.64	135.30	2.63	8.39
*3-Month OL	n	96	96	94	94	92	92	92	92
	Mean	128.2	130.3	-2.9	-5.8	-140.9	134.0	-1.7	-7.4
	SD	137.98	144.40	4.32	10.15	156.42	134.90	3.33	9.20
OL endpoint	**n**			**86**	**87**			**82**	**83**
1-year switch	**LSMean**	**-59.5**	**+49.7**	**-0.9**	**-2.5**	**-1.9**	**+23.1**	**0.4**	**-0.8**
	SEM	**14.4**	**18.7**	**0.49**	**0.72**	**14.6**	**19.0**	**0.49**	**0.72**
	p-value	**0.0040**	**0.0108**	**0.0719**	**0.0016**	**0.9007**	**0.2658**	**0.403**	**0.2901**

FAS, full analysis set; DB, double-blind; ENT, entacapone; OL, open-label; OPC, opicapone; LS Mean, Least square mean from MMRM with Region and Visit as factor and DB Baseline as covariate; SD, standard deviation; SE, standard error

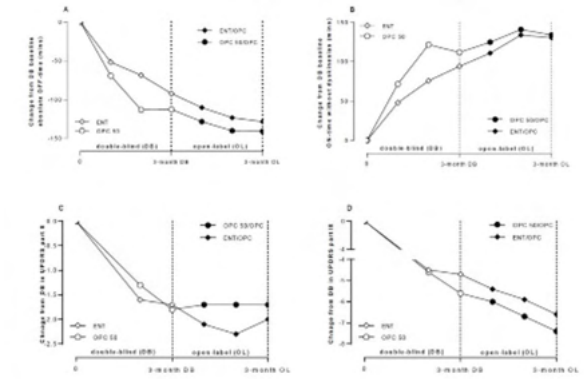

Figure 1. Change from double-blind baseline to 3-month open-label, by previous double-blind treatment (FAS): A, Absolute OFF-time; **B**, ON-time without dyskinesias; **C**, UPDRS part II; **D**, UPDRS part III
DB, double-blind; ENT, entacapone; OPC, opicapone

Conclusion: These data suggest that early rather than delayed addition (or second-line) of OPC 50mg to levodopa/DDCI provides an extended benefit over ENT.
Disclosure: 1.Ferreira et al., Lancet Neurol. 2016;15(2):154-165; 2.Lees et al., JAMA Neurol. 2017;74(2):197-206.

EPO-298

Motor and non-motor symptoms in the early post-transplant period compared with placebo therapy in Parkinson's disease

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Background and aims: Parkinson's disease (PD) is a chronic, progressive neurodegenerative disease. The use of mesenchymal stem cells (MSCs) is a perspective method to influence the pathogenesis of the disease. However, the influence of the possible placebo effect on therecovery process has not been fully investigated. The clinical transplantation study that has started in January 2019 so far included 16 PD patients in the post-transplant period and 13 patients from control group that received placebo therapy.
Objective: To compare the early results of the introduction of MSCs and placebo on the dynamics of the motor and non-motor symptoms in patients with PD.
Methods: MSCs were transplanted to 16 patients with PD via tandem (intranasal + intravenous) injection. Placebo therapy (isotonic saline) was performed to 13 patients with PD via tandem injection. Effectiveness of the therapy was evaluated one and three months post-transplantation according to the dynamics of non-motor symptoms by scoring the following scales: The Montreal Cognitive Assessment, Hamilton Depression Rating Scale, The Pittsburgh Sleep Quality Index, The Epworth Sleepiness Scale, Non-Motor Symptoms Scale, The 39-item Parkinson's Disease Questionnaire. The severity of motor symptoms was evaluated on the basis of Section III of the Unified Parkinson's Disease Rating Scale.
Results: The severity of motor and non-motor symptoms in the post-transplant period decreased in contrast to the control group.
Conclusion: Our results of the introduction of MSCs on the intensiveness of the motor and non-motor symptoms in patients with PD significantly exceed the placebo effect.
Disclosure: The research was carried out from the task "Development and implement a Parkinson disease therapy method using cellular technologies" (the subprogram of the State scientific-technical program "New methods of medical care").

EPO-299

Clinical use of botulinum toxin for reducing autonomic symptoms of Parkinson's disease: a systematic review

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Background and aims: Botulinum toxin (BoNT) is well tolerated in reducing many autonomic symptoms, upholding different benefits such as reduction of medication use, longer action time and quality of life improvement. In this systematic review, we explored the clinical use of BoNT for reducing different autonomic symptoms of Parkinson's disease: sialorrhea, neurogenic bladder and constipation.
Methods: Papers were selected searching the PubMed, Medline and Cochrane Library databases based on the descriptors: "sialorrhea" OR "neurogenic bladder" OR "constipation" AND "botulinum toxin" AND "parkinson". The inclusion criteria was limited to clinical trials or randomized controlled trials that evaluated the efficacy of BoNT in managing autonomic symptoms of patients with Parkinson's disease.
Results: Among the 101 papers initially identified, only 10 were eligible for the review after full texts were read. The efficacy of BoNT was mostly observed in sialorrhea and hyperhidrosis, with up to 88% patients having symptoms reduced for six to nine months with at least two class 1 studies attesting its validity. It was also documented gastrointestinal dysfunction (gastroparesis and constipation) reduction in up to 77% patients throughout four months. Finally, BoNT was also effective in urinary dysfunction, with up to 71% of patients having LUTS (low urinary tract symptoms, such as nocturia and urgency) reduced.
Conclusion: Studies analysis suggests that the therapeutic use of BoNT is efficient and safe while treating Parkinson's autonomic symptoms, especially sialorrhea. BoNT allows to expand the methods that improve patients' quality of life, without the side effects related to traditional pharmacological treatments.
Disclosure: Nothing to disclose.

EPO-300

Opicapone OASIS study in Parkinson's: design of an open-label, single-arm, pilot trial

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Background and aims: Opicapone proved to be effective in the treatment of end-of-dose motor fluctuations in Parkinson's Disease (PD) patients [1,2]. Non-motor symptoms have a substantial impact on health-related quality-of-life and are reported in about 90% of idiopathic PD patients [3]. End-of-dose motor fluctuations and associated sleep disorders are commonly observed in PD patients under treatment with L-dopa/DOPA decarboxylase inhibitors (DDCI). Therefore, there is the expectation that opicapone might improve such symptoms.
Methods: Approximately 30 patients (aged 30 years) with idiopathic PD, treated with 3-8 daily oral doses of L-dopa/DDCI, with 'wearing-off" and experiencing sleep disorders will receive OPC 50mg once-daily during a 6-week evaluation-period. L-dopa/DDCI daily dose, but not number of intakes, may be adjusted according to subject response in the first 2 weeks, and kept unchanged afterwards (Figure 1). As a pilot study, no formal sample size calculation was performed.

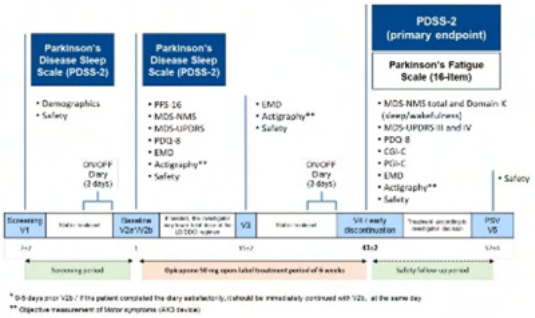

Figure 1. Overall OASIS study design.
MDS: Movement Disorder Society, UPDRS: Unified Parkinson's Disease Rating Scale, NMS: Non-Motor Symptoms, EMD: Early Morning Dystonia, PDQ-8: Parkinson's Disease Questionnaire 8-Item, PGI-C: Patient Global Impression of Change, CGI-C: Clinical Global Impression of Change, PSV: Post-Study Visit

Results: The primary endpoint is change from baseline in total score of Parkinson's Disease Sleep Scale (PDSS-2). Secondary endpoints include tolerability, functional motor and non-motor assessments [MDS-NMS, PDQ-8, Fatigue Scale (PFS-16), ON/OFF home diary] and Global Impression of Change (CGI-C, PGI-C). Study sites are in Germany and Portugal. First-patient-in is expected for 2021 and Last-patient-out to late 2021. Timelines might be impacted by COVID-19 pandemic situation.
Conclusion: This study will further evaluate the potential impact of OPC 50mg once-daily as adjunctive therapy to L-dopa/DDCI on PD-associated sleep disorders.
Disclosure: 1.Ferreira et al., Lancet Neurol. 2016;15(2):154-165; 2.Lees et al., JAMA Neurol. 2017;74(2):197-206; 3.Gökçal et al., Noro Psikiyatr Ars. 2017;54(2):143-148

MS and related disorders 2

EPO-301

Measuring the symptoms and impacts of fatigue in relapsing multiple sclerosis using a novel disease specific scale

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Background and aims: Fatigue is among the most frequent and disabling symptoms in relapsing multiple sclerosis (RMS) patients. A study was conducted to measure self-reported MS fatigue and its daily-life impact in a real-world population using the RMS-specific Fatigue Symptoms and Impacts Questionnaire-Relapsing Multiple Sclerosis (FSIQ-RMS).

Methods: This noninterventional prospective study recruited RMS patients on the Carenity platform across the US, with an ongoing EU expansion, projecting 375 patients from Italy, Germany, France, Spain, and UK, and will include Latin America. Participants completed the FSIQ-RMS, a 7-item questionnaire administered daily for seven days, to assess fatigue symptoms and physical, cognitive/emotional and coping impacts, with scores ranging from 0–100 (higher score=greater severity). Data on disease history, disease status, sleep, social and emotional functioning, were also captured. Follow-up assessments at six and 12 months are planned following the same pattern.

Results: Among the 300 RMS US participants: mean age: 43.0 years; 88% women; mean diagnosis age: 32 years. Fatigue was reported as the symptom having the greatest impact on daily life and was rated as severe, mean score 57.3 for the FSIQ-RMS symptoms domain and 42.3, 43.4 and 50.1 for the three impacts subdomain scores: physical, cognitive/emotional, and coping. Fatigue severity did not vary across disease duration or disease-modifying therapy categories (Figure). Fatigue had the highest impact on ability to perform daily activities (6.9/10) and on professional life (4.5/10), among those currently employed (48%) (Table).

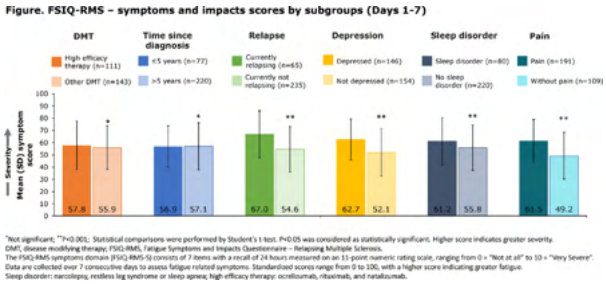

Figure. FSIQ-RMS – symptoms and impacts scores by subgroups (Days 1-7)

Figure

Table. Impact of fatigue on various aspects of daily life

Characteristic	N=300
Impact of fatigue on different aspects of life, mean (SD) score	
Ability to perform daily activities	6.9 (2.7)
Social life	6.8 (3.1)
Emotional well-being	6.5 (2.8)
Professional life	6.0 (3.7)
Family life	5.8 (3.0)
Impact of fatigue on professional life, mean (SD) score	**n=145**
Professional life in general	4.5 (3.4)
Presenteeism	4.4 (3.3)
Productivity at work	4.3 (2.9)
Well-being at work	4.3 (3.0)
Mean through all aspects	4.0 (2.6)
Career advancement	3.9 (3.6)
Quality of work	3.8 (3.1)
Absenteeism	2.6 (3.1)
Among participants working full-time	*n=100*
Presenteeism	4.4 (3.3)
Productivity at work	4.0 (2.9)
Well-being at work	3.9 (2.9)
Professional life in general	3.8 (3.0)
Mean through all aspects	3.6 (2.5)
Quality of work	3.4 (2.9)
Career advancement	3.3 (3.5)
Absenteeism	2.2 (2.7)

The impact of fatigue on several aspects of patient's life was rated from 0 (no impact) to 10 (very high impact).

Table

Conclusion: Fatigue occurred in most MS participants and adversely influenced patient's daily life. The assessment data for EU participants will be presented.

Disclosure: OW is an employee of Carenity; MS, LL, EK are employees of Janssen; LEC is a former employee of Janssen; LBK received personal fees from from Sanofi Aventis, Biogen, Novartis, Gerson Lehrman, EMD Serono, Allergan Inc., and Tesaro Inc.

EPO-302

Clinical predictors of "benign" progression in Multiple Sclerosis

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Background and aims: Predicting disease progression remains a challenge in the management of Multiple Sclerosis (MS). While highly debated, the term "benign" is often used to describe forms of the disease that evolve slowly with lower functional burden. Gender, age at onset, number of relapses in the first year, interval between relapses, and early pyramidal involvement have classically been described as markers of prognosis.
Methods: We aimed to identify clinical and demographic aspects predicting milder course, defined as EDSS score3.0 at 15 years. We reviewed clinical records of a cohort of 200 MS patients with at least 15 years of disease duration. Patients with progressive forms at onset were excluded. Clinical variables selected included site of involvement of first relapse, number of relapses in first year, and time between first symptoms-diagnosis, first to second relapse, and diagnosis-therapy initiation.
Results: Patients were 67.5% (135) female, mean age at onset 28,35±10,42 (6–40) and mean disease duration 23±7 years. Mean interval from diagnosis to therapy was 120,05±99,07 (0–582) months. Number of relapses in the first year ranged from 1–4. Brainstem symptoms at presentation were most common (26.7%), followed by optic neuritis (21%), supratentorial (19.9%), spinal (18.8%) and multifocal (13%) involvement. At 15 years of disease, 53% patients had an EDSS score 3.0.
Conclusion: Only two variables negatively predicted outcome: age at onset (p=0.006) and delay to therapy initiation (p=0.008). In our cohort there was no correlation between most "classical" markers of worse prognosis and higher long term EDSS score. Unfortunately, neuropsychological evaluation was not consistently available in this patient cohort, which precluded retrospective analysis of cognitive impairment as either an early marker or outcome measure.
Disclosure: Nothing to disclose.

EPO-303

The course of COVID19 in patients with multiple sclerosis (MS) receiving anti-B-cell therapy

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Background and aims: During the pandemic, patients with MS receiving immunosuppressive therapy are increasingly at risk of COVID19.
Methods: We observed two patients who underwent COVID19 while using anti-B-cell therapy (at intervals between infusions). Neurological status, laboratory parameters (main subpopulations of B-lymphocytes, main indicators of general and biochemical blood tests) were regularly monitored in dynamics in each patient, and neuroimaging was performed.
Results: A patient, aged 54, with primary progressive MS, who has received anti-B-cell therapy since October 2018, had a COVID-19-associated bilateral polysegmental pneumonia of moderate severity in May 2020 with complete recovery, COVID-19 therapy was carried out in accordance with national recommendations, while dynamic observation did not show an increase in the EDSS score (4.5). A patient, aged 37, with a highly active course of relapsing-remitting MS, having received anti-B cell therapy since April 2018, had COVID-19 (mild course) in November 2020 with full recovery. COVID-19 therapy was carried out in accordance with national recommendations, while dynamic observation did not record episodes of exacerbation of MS against the background of COVID-19, and there was no increase in the EDSS score (3.5).
Conclusion: It is important to note that according to the available laboratory data, both patients underwent COVID-19 against the background of severe depletion of CD20 B-lymphocytes (according to the dynamic phenotyping of B-lymphocytes, the absolute number of CD19 cells was 0). The course of the disease did not have any special features compared to the general data on the population. Both patients continue anti-B-cell therapy, their condition remains stable, dynamic observation continues.
Disclosure: Nothing to disclose.

EPO-304

Experience in the management of pregnant women with aggressive multiple sclerosis (MS) receiving natalizumab therapy

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Background and aims: Until recently, when women with MS became pregnant, disease-modifying therapy was usually canceled. However, in patients with an aggressive course of the disease, when therapy is discontinued, activity of the disease usually resumes.
Methods: We observed five pregnant patients with aggressive MS treated with natalizumab. For two of them therapy was stopped at the beginning of pregnancy, for the others – treatment was extended to 30 weeks of pregnancy.
Results: In the first patient, natalizumab therapy was discontinued at five weeks of pregnancy. At week 17 an exacerbation stopped by hormones was registered. The second patient received natalizumab until the 9th week of pregnancy. After discontinuation of therapy, two exacerbations occurred at 13 and 24 weeks of pregnancy. Exacerbations were stopped by methylprednisolone. Both patients gave birth on time, healthy children with normal body weight. Since 2019, the infusion of natalizumab has been allowed until the 30th week of pregnancy. We observed three pregnant patients who received natalizumab before the 30th week of pregnancy. In one patient, the titer of AB to JCV was >1.5. Infusions were performed with an extended interval of administration: one time in six weeks. None of the patients had any exacerbations during pregnancy, and hormone therapy was not performed. All of them had healthy full-term babies with normal body weight.
Conclusion: During pregnancy in patients with aggressive MS treated with natalizumab, therapy with this drug is safe to carry out up to 30 weeks of pregnancy. At the same time, no negative effect on the fetus was registered.
Disclosure: Nothing to disclose.

EPO-305

Oligoclonal band patterns in neurological diseases

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Background and aims: Qualitative detection of CSF imunoglobulins(IgG) by oligoclonal bands(OCB) positivity is usually associated with inflammatory neurologic diseases(ID). Their relevance in other neurological diseases is poorly recognized.
Objectives: To describe OCB patterns in patients with suspected ID and its relation to clinical/etiological diagnosis.
Methods: Retrospective analysis of patients with positive CSF OCB by isoeletric focusing, in a tertiary hospital between 2015–2016. Classification of OCB patterns according to the international consensus (pattern 2-OCB in CSF only, 3-CSF>serum, 4-CSF=serum) and final diagnosis as ID, NID(non-inflammatory neurological disease), U(undetermined etiology) and NN(non-neurologic). Comparative analysis by Kruskal-Wallis (continuous variables) and chi-square(categorical variables).
Results: We evaluated 283 patients, 54,4% females, mean age=56 (±19,2) years-old at CSF collection. Pattern4 was observed in 138 (48.8%) patients, 83 (29.3%) pattern2 and 62 (21.9%) pattern3. Most frequent clinical syndrome in pattern2 was long tract and brainstem involvement, in pattern4 was dementia, and in pattern3 was long tract ($p<0.001$). Median of CSF cells=2/l (min0–max691) and median IgG index=0.62 (0.02–3.81), pattern4 presenting lower values versus patterns2/3 ($p<0.001$). ID was the final diagnosis in 145 (51.2%), NID 95 (33.6%), U 39 (12.8%) and NN 4 (1.4%). Uppermost ID were: primary autoimmune disorders of the nervous system(NS), including demyelinating disease, encephalitis, CNS vasculitis and peripheral neuropathies (88/145); systemic autoimmune disorders with NS involvement (26) and CNS infections (22). NID were: neurodegenerative (32/95), vascular (18), toxic (13). Most pattern2 and three had an ID (75.9 e 62.9%) while in pattern4 prevailed NID (47.8%) ($p<0.001$).
Conclusion: OCB are present in CSF in an important group of non-inflammatory neurological diseases. The result of this paraclinical test should be integrated into the clinical picture and the OCB pattern may be useful in guiding the investigation.
Disclosure: Nothing to disclose.

EPO-306

Clinical case presentation of a possible oligodendroglioma-related paraneoplastic CNS demyelination syndrome

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Background and aims: Paraneoplastic neurological syndromes mediated by T-cells or antibodies occur after an immune diversion towards nervous system elements following a malignancy. Our objective is to report a rare case of possible paraneoplastic CNS demyelination.
Methods: Clinical examination, review of history, radiological, serological and CSF investigation.
Results: A 39-year-old female carrier of a BRCA2 mutation linked to increased risk of several types of malignancies was examined in our outpatient department presenting with asymmetrical bilateral leg paraesthesia. MRI revealed multiple CNS inflammatory lesions as well as a tumorous lesion which was initially considered to be a tumefactive demyelinating lesion but was later proven histologically to be an oligodendroglioma. CSF examination showed oligoclonal bands. Based on her clinical history, MRI and CSF findings a diagnosis of multiple sclerosis was established and the patient was treated with rituximab leading to symptomatic improvement. Paraneoplastic markers revealed low-titre anti-CASPR2 antibodies in the serum and elevated levels of CXCL13 in the CSF.
Conclusion: Anti-CASPR2 antibodies can be paraneoplastic and are mostly associated with limbic encephalitis and peripheral hyperexcitability , but other clinical phenotypes have also been postulated. The location and function of the CASPR2 protein in the Ranvier juxtaparanodes could explain the involvement of the antibodies in a CNS demyelinating syndrome. Our case is an example where autoantibody production may have occurred as a result of the patient's oligodendroglioma, contributing to the observed demyelination.
Disclosure: The authors declare no relevant disclosures.

EPO-307

White matter lesions in myotonic dystrophy type 1: when a second disease co-exists

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Background and aims: Myotonic dystrophy type 1 (DM1), an autosomal dominant disorder, is clinically characterized by distal muscle weakness, myotonia, cataract and multiorgan involvement, including the CNS (sub-cortical and peri-ventricular white matter hyperintensities).
Methods: Clinical case's description.
Results: A 43-year-old woman, previously diagnosed with DM1, with symptoms begging at childhood, currently presenting a predominantly distal (3+) hypotonic tetraparesis, neck flexor weakness, cataract and slight respiratory involvement. She was admitted with hypoesthesia below the waist, worsening of previous lower-limb muscular weakness, progressing to walk inability without support in one week. Retrospectively, she reported an episode, occurred 21 months earlier and lasting two months of numbness below the waist. On examination, we found, a de novo, patellar hyperreflexia, left Babinski sign and sensory loss level below T12. A brain and medulla MRI revealed multiple demyelinating lesions characteristics with a periventricular, juxtacortical, infratentorial and spinal cord location. A tumefactive oval lesion, posterolateral, at C5–6, with gadolinium enhancement was seen. Several other supratentorial coexisting lesions showed gadolinium enhancement. CSF analysis detected a normal glucose, cell count and proteins level, an elevated IgG index and the presence of oligoclonal bands. Visual evoked potentials showed a left optic neuropathy. The diagnosis of Relapsing-remitting Multiple Sclerosis (MS) was assumed and Natalizumab was started.
Conclusion: In this case, the presence of clinical, imaging and laboratory criteria allowed the diagnosis of MS. Despite the multisystemic nature of DM1, other unrelated pathologies can occur and need to be considered. So far, there are few reported cases of simultaneous occurrence of MS and DM.
Disclosure: No potential competing interest was reported by the authors.

EPO-308

Fingolimod and natalizumab – is there a role of the follow-up drug in the occurrence of rebound?

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Background and aims: Suspension of disease-modifying-drugs (DMDs) in MS can lead to rebound (occurrence of a severe relapse or significantly higher clinical/radiological disease activity compared with pre-treatment levels). Lymphocyte traffic-blockers, fingolimod and natalizumab, are most commonly implicated in rebound. While longer washouts are associated with increased rebound risk, less is known about the contribution of the follow-up treatment for its occurrence.
Methods: We hypothesized that the deleterious effects of the massive entry of activated T and B-cells into the brain parenchyma after a long traffic-blocker washout might be potentiated by follow-up treatments that suppress B-regulatory activity, leaving activated T-cells unchecked and prompting a severe return of neuroinflammation. The records of all patients from our centre that switched from traffic-blockers until December 2019 were reviewed.
Results: Overall, 24 patients (14 female;mean age:39) switched from fingolimod and 21 (10 female;mean age:42) from natalizumab. Median disease duration was higher (10 vs 8.5 years) and ARR (year before switching) lower (0vs1) in the natalizumab group, while EDSS was similar (3.5). We had five rebounds (17% after fingolimod; 5% after natalizumab). Independently of the follow-up drug, all five rebounds occurred in a group with longer (>6 weeks) washouts (25%): four switching to anti-CD20 (out of 9;45%) and one to cladribine (out of 3;33%); none of the remaining patients, switching to other DMDs, had rebound.
Conclusion: Our results confirm the importance of short-term washouts to minimize rebound. Despite its limitations, they suggest that when switching from traffic-blockers to anti-CD20 or cladribine, extra-caution should be put in avoiding long washout periods to avoid rebound.
Disclosure: Nothing to disclose.

EPO-309

Fatigue in patients with multiple sclerosis

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Background and aims: Multiple sclerosis (MS) is chronic neurological autoimmune disorder. MS fatigue is one of the most common and most disabling nonmotor symptoms, affecting almost 80% of the patients and influencing negatively on the quality of the life (QoL). We aim to examine severity of fatigue in MS patients, it`s relationship with demographic parameters, disease type and immunomodulatory therapy and to evaluate it`s impact on the QoL.
Methods: Patients were surveyed for demographic data and treatment using self-created questionnaire. Motor symptoms were evaluate using Expanded Disability Status Scale (EDSS). Symptoms of fatigue and QoL was assessed using a Modified Fatigue Impact Scale (MFIS) and a Quality of Life Questionnaire for MS patients (MS QoL-54).
Results: 30 MS patients were evaluated. Most of the patients felt fatigue. Age, the age at disease onset and EDSS positively correlated with the fatigue scale. Married patients reported a higher degree of fatigue. Patients who report a higher degree of fatigue are more likely to have temporary or permanent incapacity for work. We did not observe a difference in the fatigue severity in regard to MS types nor immunomodulatory therapy. Fatigue symptoms negatively correlate with overall QoL and with all individual domains of QoL.
Conclusion: Most of the patients experiance fatigue. Age, older age at the time of disease onset, and the severity of motor symptoms negatively influence on fatigue symptoms. Married patients have a more pronounced fatigue, and fatigue has a negative effect on work ability and the QoL.
Disclosure: Nothing to disclose.

EPO-310

Evaluation of specific unmet medical needs in the care of relapsing MS: Interim analysis of the PROFILE RMS study

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Background and aims: Although several disease modifying treatments (DMTs) are currently available for relapsing multiple sclerosis (RMS), there are patients with unmet medical needs. Thus, to improve therapy for these populations, PROFILE RMS (ML39348) aims to characterize the real-world treatment of patients in five pre-defined profiles with unmet medical needs (Table 1).

Methods: The prospective, non-interventional study PROFILE RMS will enroll 1,215 patients at ~100 centres in Germany. Patients 18 years old with RMS (relapsing remitting or relapsing secondary progressive MS) according to McDonald 2010 criteria that are treatment naïve or formerly/currently treated with DMTs according to local labels will be included. The primary outcome is the 48-week failure rate (defined as confirmed relapse, EDSS progression, MRI activity or treatment change). Secondary outcomes include the proportion of patients with treatment change, patient-reported outcomes, and MS signs and symptoms (complete list in Table 2).

Group	Profile
1*	Disease activity on current DMT in the past 12 months (occurrence of confirmed relapse, new/enlarged MRI lesions, or disease progression)
2*	Significant side effects (infections, injection problems) or findings of theoretical safety concerns as assessed by the treating physician
3*	Low treatment satisfaction (measured by the Treatment Satisfaction Questionnaire for Medication version 1.4 Global)
4	Treatment-naïve
5*	Previously treated with DMT, but no current treatment

*Following medications included: glatiramer acetate, beta-interferons, dimethyl fumarate, teriflunomid, fingolimod, alemtuzumab, natalizumab, peginterferon, cladribin, mitoxantron, ocrelizumab, daclizumab (retrospectively up to 2 March 2018); DMT, disease modifying therapy; MRI, magnetic resonance imagery.

Table 1. Patient profiles used to identify unmet medical needs in PROFILE RMS

Group	Profile
Effectiveness	
Primary	48-week failure rate as defined by confirmed relapse, EDSS progression, MRI activity, or treatment change
Secondary	Time to confirmed relapse and proportion of relapse-free patients at the end of the study
	Change from baseline EDSS score and time to EDSS progression
	Proportion of patients with treatment change and types of treatments from which the patient switched
	Change in patient/physician adapted global impression of disease course
	Change in quality of life and patient-reported treatment satisfaction (measured by HR-QoL, WPAI:MS, MSIS-29 version 2 and TSQM)
	Change in multiple sclerosis signs and symptoms (measured by 2-minute walking test, SDMT, FSMC and HADS)
Safety	Frequency and severity of adverse events (AEs), serious AEs, and AEs of special interest.

EDSS, The Expanded Disability Status Scale; FSMC, Fatigue Scale for Motor and Cognitive Functions; HADS, Hospital Anxiety and Depression Scale; HR-QoL, health-related quality of life; MRI, magnetic resonance imaging; MSIS-29, Multiple Sclerosis Impact Scale-29; SDMT, Symbol Digit Modalities Test; TSQM, Treatment Satisfaction Questionnaire for Medication; WPAI:MS, Work Productivity and Activity Impairment Questionnaire

Table 2. Effectiveness and safety outcome in PROFILE RMS

Results: As of 4th November 2020, 691 patients were included in this analysis of which 79.7% were female with a mean (range) age of 43.4 years (19–80). Of patients currently on treatment (profiles 1–3; n=405), the most common reasons for the first treatment change (14.8% of patients) were ongoing disease activity (5.2%), low treatment satisfaction (3.5 %) and other (3.2%) (Table 3). Data for the effectiveness and safety outcomes will be presented at the congress.

	Profile 1 (n=234)	Profile 2 (n=112)	Profile 3 (n=59)	Combined (n=405)
Patients with treatment change (%)	33 (14.1)	19 (17.0)	8 (13.6)	60 (14.8)
Reasons for first treatment change				
Adverse events	3 (1.3)	2 (1.8)	-	5 (1.2)
Dose change	-	1 (0.9)	-	1 (0.2)
Low quality of life	-	3 (2.7)	2 (3.4)	5 (1.2)
Low treatment satisfaction	7 (3.0)	4 (3.6)	3 (5.1)	14 (3.5)
Ongoing disease activity	15 (6.4)	4 (3.6)	2 (3.4)	21 (5.2)
Other	8 (3.4)	4 (3.6)	1 (1.7)	13 (3.2)
Safety concerns	-	1 (0.9)	-	1 (0.2)

Profile 1, Disease activity on current DMT in the past 12 months (occurrence of confirmed relapse, new/enlarged MRI lesions, or disease progression); Profile 2, significant side effects (infections, injection problems) or findings of theoretical safety concerns as assessed by the treating physician; Profile 3, low treatment satisfaction (measured by the Treatment Satisfaction Questionnaire for Medication version 1.4 Global).

Table 3. Reasons for first treatment change in patients from profiles 1, 2 and 3

Conclusion: We will present the first ever safety and effectiveness data from PROFILE RMS, a study aiming to provide insights into the care of RMS patients with unmet medical needs in Germany.

Disclosure: IKP: Adamas Pharma, Almirall, Bayer Pharma, Biogen, Celgene, Genzyme, Janssen, Merck, Novartis, Roche, Teva // speakers bureau or advisory board, consulting fees; The German MS Society, Celgene, Novartis, Roche, Teva // research grants.

EPO-311

Post-vaccination medulla oblongata encephalitis with selective trigeminal involvement: clinical presentation

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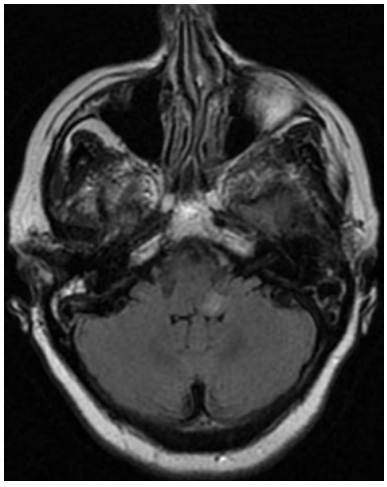
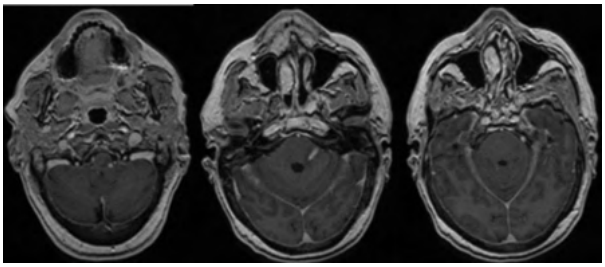
Background and aims: Acute disseminated encephalomyelitis (ADEM) is a rare, immune-mediated disease, usually following an infection or vaccination, clinically defined by acute onset of multifocal neurological deficits, and more frequent in the pediatric population. Clinical forms without encephalopathy and monofocal involvement are even rarer and depend upon the location and the degree of demyelination within the central nervous system.

Methods: We present the case of a 64-year-old female, who was vaccinated for influenza and pneumococcus one week before symptoms onset, that was admitted for paresthesias on her left face evolving over three days; preceded four days before by intense dizziness, unilateral left headache, acute left ear and left neck pain. Her neurological examination revealed only diminished pinprick sensation limited to the distribution of the left trigeminal nerve. During hospitalization, she also described the loss of taste on the left side of the mouth cavity.

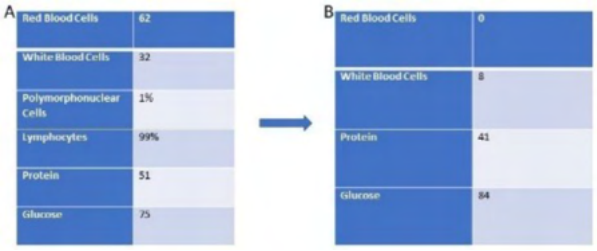
Results: Magnetic resonance imaging (MRI) results are shown in figures 1 and 2. Cerebrospinal fluid (CSF) showed a pattern suggestive of inflammation. The patient recovered progressively before MRI, so we didn't initiate any treatment. At discharge, only mild hypoesthesia on the left malar region remained, and CSF values normalized (Figure 3).



Brain MRI FLAIR sequence revealing hyperintensity on the left medullary region and the left trigeminal nerve.



Brain MRI T1-weighted postcontrast sequences showing enhancing throughout the left trigeminal nucleus, with almost selective involvement of the left trigeminal nerve.



A, CSF results of the first lumbar punction. B, CSF results after three days, showing improvement of parameters.

Conclusion: ADEM is a very rare illness in adults and is considered a diagnosis of exclusion. Patients characteristically present with encephalopathy. Focal presentation in post-vaccination encephalitis is rather heterogeneous but neurological deficits especially if closely timed to an immunization should alert the clinician to its possible diagnosis.

Disclosure: Nothing to disclose.

EPO-312

Lymphopenia In Multiple Sclerosis Patients Under Dimethyl Fumarate – The Experience Of a Portuguese Center

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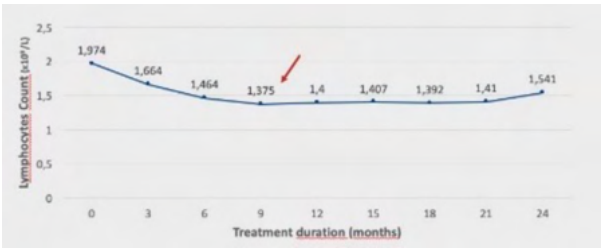
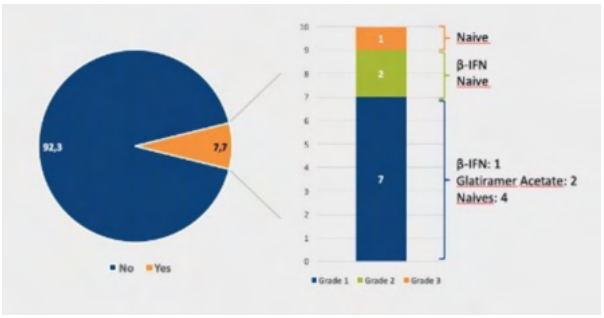
Background and aims: Dimethyl Fumarate (DMF) is an oral disease-modifying therapy approved for management of relapsing-remitting multiple sclerosis (RRMS) patients. It has been associated with unpredictable reduction in absolute lymphocyte count (ALC), so it is recommended to perform white blood cell count before starting treatment and thereafter performed quarterly. Our aim is to evaluate ALC in patients with RRMS.

Methods: Retrospective study including patients with RRMS, at least with 12 months of DMF treatment and analytical study conducted at our center. ALC were evaluated quarterly, assigning degrees of lymphopenia according to Common Terminology Criteria for Adverse Events: Grade 1 0.99–0.8x109/L; Grade 2 0.79–0.5x109/L; Grade 3 <0.5x109/L.

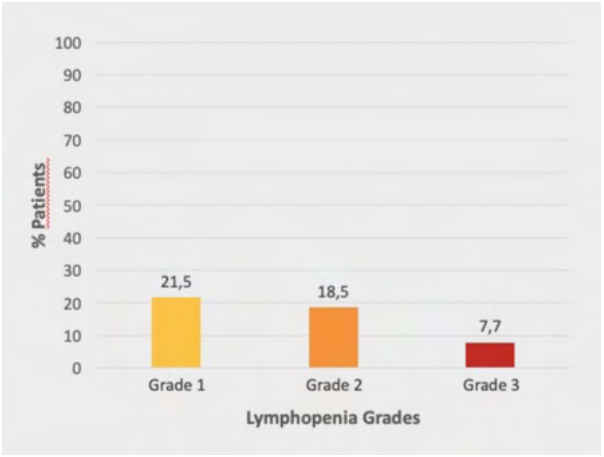
Results: We included 130 patients, 69.2% female, with mean age of 36.13 years-old and mean duration of DMF treatment of 31.38 months. 51.7% took other disease-modifying drugs. At pretreatment evaluation, 7.7% of patients had lymphopenia (7 grade 1; 2 grade 2; 1 grade 3): six were naïve, four had other drugs (2 interferon-beta; 2 glatiramer acetate). During DMF therapy, 21.5% of patients had grade 1 lymphopenia, 18.5% grade 2 and 7.7% grade 3. There was a mean decrease of 30.34% in lymphocytes level, with a minimum value at 9th month (mean 1.38x109/L), mostly with subsequent normalization. DMF withdrawal due to severe lymphopenia occurred in 3.8% (n=5).



Lymphocytes Count with 24 months of Treatment Duration



Lymphopenia at Pretreatment Evaluation



Lymphopenia Grades during Treatment

Conclusion: ALC was stable in the patients' majority over the observed period, being the percentage of severe lymphopenias relatively low, comparable to what was described in literature.

Disclosure: Authors have no conflict of interest to declare.

EPO-313

Te complex rehabilitation of locomotor function in patients with multiple sclerosis

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Background and aims: Multiple sclerosis (MS) is a severe progressive disease that leads to disability in people of working age. MS is accompanied by a different combination of symptoms; motor disorders and balance impairment are the frequent manifestations. The possibility of restoring motor functions, as well as improving the patient's quality of life, prompts the search for new and most effective rehabilitation methods. Aim – to study the efficiency of rehabilitation measures using lower limb exoskeleton and stabilometric platform in patients with MS.
Methods: There were involved 20 patients diagnosed with MS. EDSS was varied from 4.5 to 6.5 points. The average age of patients was 44±1,5 years. The outcome measures included The Montreal Cognitive Assessment (MOCA), 6-minute walk test (6MWT), Timed 25-Foot Walk (T25FW) and Berg balance scale (BBS). Patients were conducted 10 sessions on exoskeleton and 10 sessions on stabilometric platform.
Results: All patients tolerated rehabilitation procedures well, vital signs were stable throughout the course. Data was obtained: an 0,7 sec ($p<0,05$) improvement in the 25FW score. In 6MWT the distance increased by nine meters ($p<0,05$). The improvement in BBS was 1,2 points ($p<0,05$). Improvement was found in the assessment of cognitive functions on the MOCA, which was 1,3 points ($p<0,05$).
Conclusion: The study showed an efficiency of the combined using of an exoskeleton and a stabilometric platform with biofeedback in the rehabilitation of patients with MS. A positive effect on the restoration of walking function and balance support after the course was noted.
Disclosure: There is not conflict of interest.

EPO-314

The effect of bright light therapy on fatigue in Multiple Sclerosis patients – a randomised controlled trial

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Background and aims: In patients with Multiple Sclerosis (MS), fatigue is a common disabling symptom and pharmacological treatment options remain insufficient. Bright light therapy (BLT) is an easy-to-apply intervention with few side effects and has been shown to improve fatigue in several neuropsychiatric conditions. We aimed to investigate the effect of BLT on MS-related fatigue.
Methods: Adult MS patients with severe fatigue (>35/63 points on the Fatigue Severity Scale (FSS)) were randomised into an active group (BWL; bright white light, 10.000 lux) or a control group (DRL; dim red light, <300 lux). The intervention consisted of daily light exposure (BLT or DRL) in the morning for 30 minutes. Fatigue was assessed at baseline and after the intervention with the FSS and the Modified Fatigue Impact Scale (MFIS).
Results: So far, 20 participants (80% female, mean age=43±12.5 years, mean EDSS=2.86±1.92) were enrolled; 19 were randomised and included in this analysis (10 in the active group, nine in the control group). A Wilcoxon Signed-Ranks Test indicated a trend toward significance in the active group ($Z=-1.9$, $p=0.058$) with a mean of 43.7±6.1 before and 37.6±12.4 points on the FSS after the intervention. The subscore for cognitive fatigue on the MFIS improved significantly in the active group ($Z=-2.1$, $p=0.036$). In the placebo group, the total MFIS score improved significantly ($Z=-2.075$, $p=0.038$).
Conclusion: BLT improved MS-related fatigue in our sample. Nevertheless, interpretation of these results needs caution due to the observed placebo effect and the small sample size.
Disclosure: funded by Oesterreichische Nationalbank (OeNB). No other conflicts of interest.

Muscle and neuromuscular junction disease 2

EPO-315

Atypical dermatomyositis

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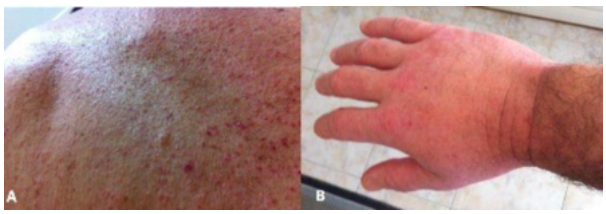
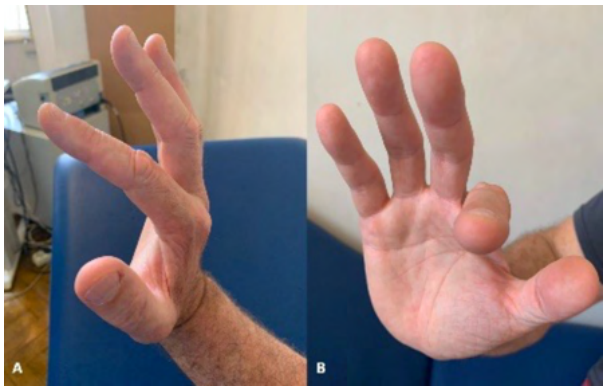
Background and aims: Dermatomyositis (DM) is an inflammatory myopathy usually characterized by symmetrical proximal muscle weakness in association with skin changes.

Methods: We report a DM patient with an unusual symmetric distal upper limb muscle weakness pattern.

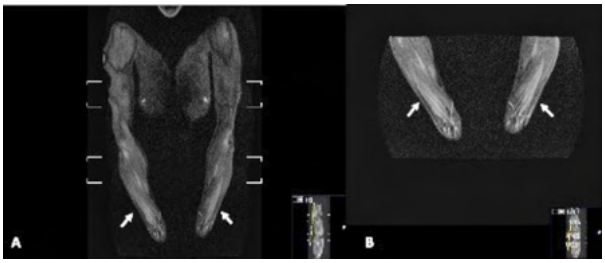
Results: A 56-year-old male presented with muscle weakness of the 2nd and 5th fingers of the right hand, three years after the appearance of different types of skin lesions. The weakness progressed, in few months, to the remaining right and left-hand fingers. On neurological examination, he presented a symmetric and distal upper limb muscle weakness pattern [Medical Research Council score of 2/5 in extensor indicis proprius, 3/5 in the remaining fingers extensors, 3/5 in abductor pollicis longus and 3/5 in all interosseus hand muscles, bilaterally]. Serum creatine kinase was slightly elevated and anti-Mi2a antibodies tested positive. Needle sampling identified a myopathic pattern in the extensor indicis proprius and abductor pollicis longus bilaterally. Right deltoid muscle biopsy was unrevealing. Upper limbs muscle MRI showed selective STIR hyperintensity in extensor muscles on both sides. Screening for occult malignancy was unremarkable. To date, the patient remains stable with low dose prednisolone plus methotrexate.



A - Skin lesions on the patient's back. B –Patient right hand presenting focal oedema.



A and B. Severe extensor indicis proprius weakness was observed in both hands.



A e B. Muscle MRI of upper limbs. Coronal STIR sequence showing bilateral high signal changes in extensor muscles, suggestive of muscle oedema (arrows).

Conclusion: DM diagnosis is dependent on clinical findings supported by complementary exams. In our patient, it was based on the preceding skin manifestations associated with distal upper limb weakness with both needle EMG and muscle MRI supportive of a distal inflammatory myopathy. The absence of DM histopathological findings was probably due to proximal muscles sparing effect. Moreover, anti-Mi2a antibody tested positive, which further supported the diagnosis.

Disclosure: No conflict of interests.

EPO-316

Nemaline myopathy: Report of two clinical cases

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Background and aims: Late-onset nemaline myopathy is a rare muscle disorder characterized by the presence of nemaline rods in muscle fibers with symptoms presenting during the adulthood. In approximately 50% a monoclonal gammopathy of unknown significance (MGUS) is detected and in some cases are associated with HIV, rarely has a genetic origin.
Methods: We present two cases of adult-onset nemalinic disease without MGUS or HIV and pathogenic mutation.
Results: Case 1: A 42-year-old woman with a history of discoid lupus consults for subacute hypoesthesia of the left hemibody, pain and generalised weakness. EMG shows myopathy of irregular distribution. In neuroimaging demyelinating lesions appeared. In muscle biopsy nemalines are observed in the muscle fibres. Genetic study founds pathogenic variant of the MYPN gene. Case 2: A 36 year-old woman with history of progressive respiratory failure with a restrictive pattern in treatment with BIPAP and severe biventricular dysfunction consults for generalised weakness from the age of 24. Muscle biopsy is carried out, observing nemalines, and in genetic test three, variants of uncertain clinical significance in MYPN was found
Conclusion: Nemaline myopathies are a varied group of muscular disorders that usually present from birth, although some cases appear in adulthood. The presentation in adulthood is of secondary origin more frequently, being only 4% of the genetics of presentation in this age. At least twelve genes have been associated with this disease. The clinical spectrum is varied. Some cases are associated with respiratory and cardiac involvement.
Disclosure: No disclosure

EPO-317

Possibilities of ultrasound examination in myasthenia gravis (MG) and motor neuron disease (MND)

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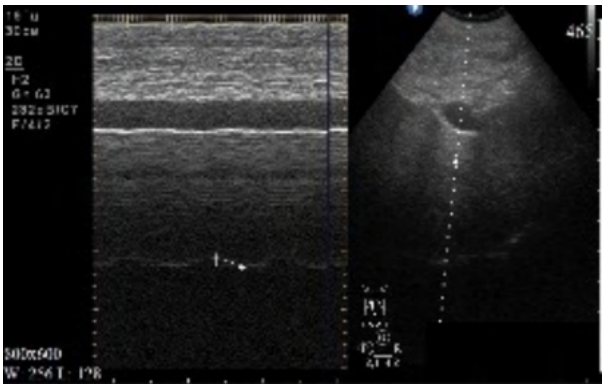
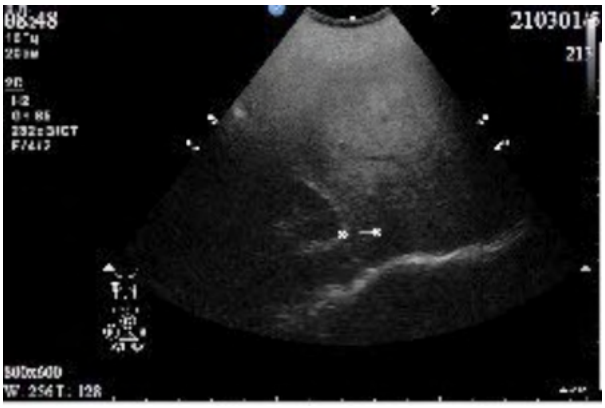
Background and aims: Detection of diaphragm violations by ultrasound is a promising direction in the early diagnosis of respiratory failure in neuromuscular diseases (NMD).
Methods: Ultrasound was performed in 65 people (27(42%) men, 38(58%) women) without signs respiratory failure, who were divided into three groups. The first group (n=15) MG patients, the second (n=16) MND patients, the third (n=34) healthy volunteers. Research was carried on HD11XE (Philips) device using sensors of linear and convexy formats, frequency 5–12 and 2–5 MHz along the midclavicular line symmetrically from two sides in the patient's supine position.



Examining of the amplitude of the diaphragm movement



Examining of the respiratory mobility of the kidneys

Results: Comparative analysis revealed significant difference between 1-3 groups: thickness of the diaphragm on the exhale left (H, $p<0.05$), thickness of the diaphragm at the end of a quiet breath left (H, $p<0.05$), thickness of the diaphragm at the end of deep breath right and left(H,$p<0.05$), amplitude of diaphragm movement during quiet breathing right and left (H, $p<0.05$), amplitude of diaphragm movement during deep breathing right and left (H, $p<0.05$), respiratory mobility of kidney during quiet breathing right and left (H, $p<0.05$), respiratory mobility of the kidney during deep breathing left (H, $p<0.05$), thickening ratio of the diaphragm left (H, $p<0.001$). Significant differences in the thickness, amplitude of diaphragm movement, respiratory mobility of the kidneys were revealed among NMD patients and healthy volunteers.
Conclusion: Significant decrease in thickness, amplitude of diaphragm movement and respiratory mobility of the kidneys in NMD were revealed, that indicates significant diaphragm violations in NMD patients.
Disclosure: Nothing to disclose.

EPO-318

Anti-HMGCR myopathy: the great mimic of limb girdle muscle dystrophy, a case report

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Background and aims: Limb-girdle muscular dystrophies (LGMDs) encompass a group of genetic disorders causing progressive weakness and wasting of the skeletal muscles, especially the proximal muscles. Some of the patients with a clinical picture of LGMD and biopsy with dystrophinopathy changes, but unrevealing genetic testing may actually suffer from Anti-HMGCR myopathy, a treatable condition that can mimic LGMD.
Methods: We studied the case of a 16 years-old female patient with a clinical picture of LGMD. The patient was examined in our clinic and muscle biopsy, Western-Blot (WB), genetic tests and antibody monitoring were performed.
Results: The 1st symptoms were noticed when she was six years old. The muscle biopsy revealed dystrophinopathy changes and the lack of dystrophin-2 was observed on WB. Whole-exome sequencing testing infirmed the diagnosis of LGMD. Antibodies against HMGCR were also tested and the level was high (73 u/ml – normal value <20 U/ml). Thus, the diagnosis of anti-HMGCR myopathy was made and we are currently planning on introducing treatment with i.v. immunoglobulins.
Conclusion: Usually, anti-HMGCR antibodies are associated with statin exposure and an acute/subacute course of the disease. Nevertheless, in some cases, it may be associated with a clinical picture of LGMD with slow progression. There are only a few such cases presented in the literature and even fewer in pediatric patients. In conclusion, considering the fact that anti-HMGCR myopathy is a treatable condition, it is important to consider it as a differential diagnosis in patients that clinically resemble LGMD but it can not be demonstrated by genetic testing.
Disclosure: Nothing to disclose.

EPO-319

Multiple mitochondrial DNA deletions associated with isolated myopathy but without external opthalmoplegia

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Background and aims: Mitochondrial DNA (mtDNA) mutations are frequently associated with multisystemic diseases. Progressive external opthalmoplegia (PEO) is one of the most common phenotypes associated with mitochondrial DNA defects including single and multiple deletions as well as point mutations. On the other hand, isolated myopathy without PEO owing to multiple mtDNA deletions is a rare clinical presentation. Such cases are not yet described in detail. A couple of congress proceedings address such patients only in abstract forms.
Methods: We report a 56-year-old male German patient with isolated myopathy but without external opthalmoplegia. COX/SDH and modified Gomori Trichome stainings were performed to access the histopathological mitochondrial defects. Long range PCR was performed to identify the mtDNA deletions in DNA extracted from blood and muscle. A panel of five genes (POLG, TWNK, SLC25A4, OPA1 and RRM2B) was investigated to identify possible molecular defects in nuclear genes.
Results: Histopathologically, COX-deficient fibres and ragged-red fibres (RRF) were moderately present in the muscle biopsy. Molecular genetic analysis identified multiple mtDNA deletions in blood and muscle samples. Molecular defects of the nuclear genes commonly associated with mtDNA multiple deletions were not identified. Exome sequencing to identify possible defects in other nuclear genes is currently underway.
Conclusion: The present case suggests that multiple deletions of mtDNA are not invariably associated with PEO but might also be present in isolated myopathy without involvement of extraocular muscles. Hence, analysis of mtDNA deletions should be performed also in patients with isolated myopathy but without PEO.
Disclosure: Nothing to disclose.

EPO-320

Decline of respiratory function in patients with dysferlinopathy (LGMD2B)

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Background and aims: To date, there is no clear evidence of respiratory decline in patients with dysferlinopathy. Few studies have evaluated this issue, and there are not detailed reports following-up respiratory function over the years. Our aim is to describe changes in forced vital capacity(FVC) in a longitudinal cohort of genetically confirmed dysferlinopathy patients and to investigate associated clinical variables. No
Methods: We performed a retrospective analysis of clinical data from all patients with dysferlinopathy assessed in our Highly Specialised Service for Muscular Dystrophies between 2002 and 2020. We collected patient demographics, FVC, presence of respiratory symptoms, need of ventilatory support and mortality. Clinical information including disease onset and duration and ambulatory status were also collected.
Results: 49 patients were reviewed; mean onset of disease was 21,08±8.8y. The mean disease duration at baseline was five years (1–20y) and the mean follow-up period was four years (1–14y). At baseline (age 34,74±13,2y) 38% of the patients had an FVC <80%, while at their last follow-up (age 38,64±14y) 47% of the patients had an FVC<80%. Involvement was considered mild (FVC=70–79.9%) in 26,5%, moderate (FVC=60–69%) in 6.1%, severe (FVC=35–50%) in 10.2% and very severe (FVC<35%) in 4.1%. The two patients with very severe impairment required nocturnal non-invasive ventilation, and one died due to respiratory failure. We observed a correlation between years of disease duration, age at loss of ambulation and an FVC<80%. None of the patients met the criteria for diaphragmatic dysfunction.
Conclusion: Based on the data of this observational study, respiratory function should be yearly evaluated in patients with dysferlinopathy, especially in advanced disease stages.
Disclosure: Nothing to disclose.

EPO-321

Assessment of the quality of life of patients with Myasthenia Gravis living in the Tomsk region

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Background and aims: Myasthenia gravis (MG) is a chronic neuromuscular disease that negatively affects the physical and psychological patient's health.
Objective: To assess the degree of social restriction of patients with MG in Tomsk region and studying correlation of quality of life with duration of the disease.
Methods: The study population consisted of 56 MG patients (14(25%) men and 42(75%) women, mean age 55,5±17,7 years); 12(21%) patients with ocular myasthenia gravis (OMG), 44(79%)-generalized myasthenia gravis (GMG). The average duration of MG was 5,4±1,5 years (OMG=4±2,9; GMG=5,9±3,4 years; p=0,72). Quality of life was assessed using the 36-Item Short Form Survey (SF-36).
Results: The categories of Physical health (PH) consists 38,1±9,9 points, Mental Health (MH) – 37,7±9,5 points. PH: OMG=43,9±11,9; GMG=36,7±9; p=0,007 MH: OMG=38,9±12,2; GMG=7,3±8,9; p=0,653 The lowest results were obtained in Role-Physical Functioning domain (RP) – 22,3±6,9 points and Role-Emotional Functioning domain (RE) – 29,7±7,2 points. RP: OMG=36,1±10,6; GMG=18,9±5,6; p=0,01 RE: OMG=37±11,3; GMG= 27,9±6,3; p=0,80 The highest results were obtained in Bodily pain domain – 61,4±31,3 points and Social Functioning domain - 57,1±23,2 points. We didn't find any significant correlations between the duration of MG and categories of SF-36.
Conclusion: The quality of life depends on the form of MG and not related with duration of disease. Patients with GMG showed the worst physical health compared to patients with OMG by SF-36 assessment. The quality of life can be related with treatment strategy. So, it's necessary to monitor PH and MH during the treatment management of patients with MG.
Disclosure: Nothing to disclose.

EPO-322

Immune-mediated necrotizing myopathy associated with statin exposure: a rare side effect of a commonly used medication

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Background and aims: Immune-mediated necrotizing myopathy (IMNM) is a distinct type of inflammatory myopathy characterised by proximal muscle weakness, elevated serum level of creatine kinase (CK), myopathic electromyography (EMG) findings and typical pathological abnormalities on muscle biopsy showing necrosis or regeneration with minimal inflammatory infiltrates. Causes include paraneoplastic, toxicity and infections. Immunogenetic risk factors and anti-HMGCR and anti-SRP antibodies are associated with IMNM.
Methods: Case report
Results: We report a case of a 58 year-old man who developed progressive proximal muscle weakness and fatigue after taking atorvastatin for three years, without improvement after treatment descontinuation. The patient denied any sensory, cranial nerve, cutaneous or respiratory symptoms. Neurological examination revealed proximal muscle atrophy, normal muscle tone, symmetrical and predominantly proximal quadriparesis, decreased tendon reflexes and positive Gower's sign. Laboratory initial workup was significant for elevated CK of 10168 U/L and positive antinuclear antibodies (ANA). Electromyography showed no abnormalities. Infections and malignancy were excluded. Corticosteroids were initiated with progressive deterioration. Muscle biopsy showed sparse inflammatory infiltrate associated with necrosis of muscle fibers, typical of necrotizing myopathy. He was positive for anti-HMGCR antibodies and the HLA-allele DRB1*11 was present. The patient was treated with monthly intravenous immunoglobulin, mycophenolate and descontinued corticosteroids, resulting in muscle weakness and CK levels improving over the following months.
Conclusion: We report a case of INMN associated with HMGCR antibodies, probably due to statin exposure. INMN are severe immunomediated myopathies, demanding early recognition for proper guidance and aggressive immunosuppressive treatment.
Disclosure: Nothing to disclose.

EPO-323

Creatine Kinase based Late Onset Pompe Disease Screening. Single-centre study

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Background and aims: Late Onset Pompe Disease (LOPD) is a chronic myopathy with multisystem involvement widely underdiagnosed at our place. The present study hopes to make a LOPD screening at a third level hospital basing on Creatine Kinase (CK) levels and reviewing clinical criteria previously described.
Methods: Prospective study with initial dry blood spot Acid Alpha Glucosidase (AAG) testing in patients with long term unexplained high Creatine Kinase (CK) levels in an hospital registry from 2014 to 2018, taking into account previous history of limb girdle myopathy, and neuromuscular respiratory alteration without any known cause. Later, those with low dry blood spot AAG was tested with whole blood AAG testing .
Results: Review of 584 patients with high CK, of which 103 were long term unexplained high CK. AAG testing was made on 40 patients, median 54.7 years (IQR 38.5,68,5). 13% were women. 23 patients (57,5%) had previous history of limb-girdle myopathy. Seven (17,5%) had low AAG in dry blood spot testing. Whole blood AAG testing was normal on six (15%) patients with one low AAG patient at whole blood testing.
Conclusion: Unexplained high CK levels could be used as a biomarker for a LOPD global population screening.
Disclosure: Sanofi Genzyme

EPO-324

The Use of MRI-traced Biomarkers on Duchenne Muscular Dystrophy Assessment

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Background and aims: The Duchenne Muscular Dystrophy (DMD) is a uncurable condition, although there are treatments that may reduce its effects and improve quality of life for DMD patients. To test and assess those therapies, biomarkers are needed; specially if their obtention is non-invasive, such as by magnetic resonance imaging (MRI). Thereby, this study has the objective to describe the use of MRI-traced biomarkers associated with DMD.
Methods: The present study is a literature review. Articles were searched via PubMed, with descriptors taken from MeSH, published from 2003 to 2021, using the formula: (Duchenne Muscular Dystrophy) AND ("Biomarkers") AND ("Magnetic Resonance Imaging" OR "MRI"). Studies which did not match the objective of this review were excluded after analysis of the title and abstract.
Results: The search resulted in 45 articles, from which 11 were selected. Cohorts and case studies proposed a semi-qualitative score, which bases itself in grading of fat infiltration and edema in different sequences. There were several studies which pointed the relation between volume/cross-sectional area on a muscular group could be a biomarker to DMD. Also, other cohorts showed quantitative results about the muscle composition and its fractions using Magnetic Resonance Spectroscopy (MRS). There were found clinical trials using those biomarkers to assess its therapies for DMD.
Conclusion: MRI can monitor DMD disease quantitatively and qualitatively, which depends on the sequences used. In contrast, its use remains underappreciated, primarily because of its cost and availability.
Disclosure: Conflict of interest: The study and its researchers are not receiving funding/assistance from any commercial organizations.

EPO-325

Therapeutic successes in congenital myasthenic syndrome (CMS)

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Background and aims: CMS comprise a heterogeneous group of diseases where neuromuscular transmission is impaired due to genetic alterations, subdivided to presynaptic, synaptic and postsynaptic types. Besides pyridostigmine, different off-label therapeutic initiatives are published, depending on the specific mutation.
Methods: Our first case is a 11-year-old Roma boy with the homozygous AChR epsilon subunit (CHRNE) 1267delG founder mutation. His mother and uncle also have mild myasthenic symptoms due to this mutation. His father is a healthy carrier. The patient's symptoms began at two months with weak crying. Later ptosis and ophthalmoparesis developed, followed by generalized muscle weakness. Pyridostigmine, corticosteroid and ephedrine therapy had no significant effect. At age ten, 3,4-diaminopyridine was administered off-label (starting dose: 3x5mg), which resulted in prompt improvement, but needed to be raised gradually up to 4x10 mg within the first year.
Results: The second case is a 6-year-old boy whose symptoms started after birth with stridor and difficulty sucking. He started to climb late, began walking at 13 months, but he could never run properly. Paralysis of the vocal cords on both sides was found and treated with laterofixation. Neuromuscular NGS panel test confirmed a compound heterozygous postsynaptic DOK7 mutation (c.1124_1127dup/c.5425_55del38). Per os salbutamol monotherapy caused partial improvement (3x0,5 mg to 3x1 mg), so we combined it with ephedrine.(2x12.5 mg), which resulted in great therapeutic success. 6MWT improved (from 110 to 147 m).
Conclusion: Our cases demonstrate that even in genetically inherited disorders, small molecules can be effective if the disease is geneticaly stratified and the right therapy is administered.
Disclosure: Nothing to disclose

EPO-326

The hereditary progressive limb-girdle muscular dystrophy type 2L (Clinical case)

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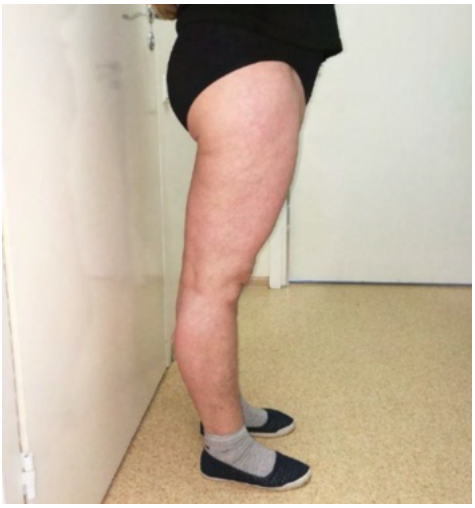
Background and aims: Limb-girdle muscular dystrophy 2L (LGMD 2L) is one of the most common anoctaminopathies and is manifested by weakness of the proximal muscles, mainly of the lower extremities.

Methods: A 55-year-old female patient was admitted to the Neurology department with complaints of gait disturbance; difficulty climbing stairs; pain in the thigh muscles. A history of gait impairment since 2013, followed by asymmetrical weakness in the legs, the patient used his hands to climb up himself. During the study medical history, somatic and neurological status, laboratory test, function testing, muscle imaging and electrophysiological data were evaluated. Muscle flap biopsy was performed to verify muscle damage.

Results: In neurological status: proximal lower limb weakness, calf hypertrophy, muscle atrophy mainly involving the pelvic girdle, hyperextension at both knees, waddling gait. Laboratory: serum CK – 1618 u/L (N 24,00–170,00). Genetic test: heterozygous mutations in the ANO5 gene; in exon 5-c. 242A>G (p.Asp81Gly), in exon 20-c.2272C>T (p.Arg758Cys). Electromyogram testing suggested the presence of a myopathy. Spirometry and echocardiography: respiratory muscles and heart were not involved. Muscle MRI demonstrated fat degeneration of most of the hip muscles, hypotrophy posterior group of muscles. Muscle flap biopsy data had no reliable signs of inflammation; non-specific signs of chronic muscle damage. According to the anamnesis, clinical, laboratory, genetic test limb-girdle muscular dystrophy type 2L was diagnosed.



Postural abnormality and a specific pose with hyperextension at both knees

Conclusion: Mutations in ANO5 represent a relatively common cause of adult onset muscular dystrophy. Screening for ANO5 is recommended in cases undetermined myopathy with a late onset, given the potential prevalence of this LGMD.

Disclosure: No disclosure

EPO-327

A fatal treatment: a case of Lambert-Eaton myasthenic syndrome as an immune-related adverse event after pembrolizumab

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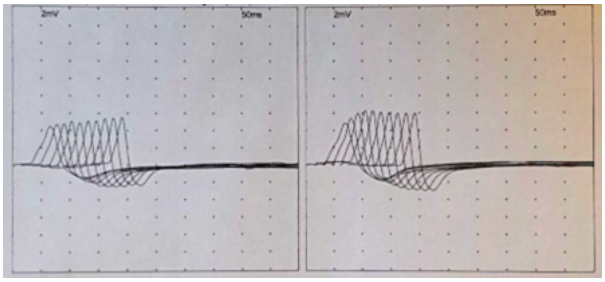
Background and aims: Pembrolizumab is an anti-programmed death-ligand-1 agent used for lung cancer treatment. Among its side effects, myasthenia gravis has been well described, and guidelines have been published on its management.

Methods: We report a patient who developed a fatal Lambert-Eaton myasthenic syndrome after pembrolizumab immunotherapy for non-small cell lung cancer.

Results: A 76-year-old man with lung adenocarcinoma presented three weeks after a second cycle of pembrolizumab with one week history of progressive lower limbs weakness which improved with resting, asthenia, dysphonia, dysphagia, right ptosis and generalized areflexia. He underwent a lumbar puncture which showed normal CSF parameters. EMG revealed no myopathic signs, despite CK 2,163UI/L, modest sensory-motor polyneuropathy, no decremental response but incremental CMAP response (20%) of the abductor digiti minimi at 20 Hz; the findings were judged compatible with Lambert-Eaton myasthenic syndrome, which had not been previously described as a neurological immune-related adverse event of pembrolizumab. Anti-acetylcholine receptor antibodies were negative, we are still waiting for anti-voltage gated calcium channel antibodies results. After multidisciplinary discussion with oncologists and anesthesiologists he was started on methylprednisolone 1g/day; due to clinical deterioration three days later with respiratory pump failure, he underwent five plasma exchange (PLEX) cycles, with only partial response. Despite treatment with NIV and oxygen therapy, he had frequent episodes of desaturation. Eventually, he developed pneumonia and died three days after the last PLEX cycle.



Repetitive nerve stimulation at 20 Hz; abductor digiti minimi response

Muscle / Trein	1st Amp mV	4 Amp %	10 Ampl %	Fac Amp %	1 Area mVms	4 Area %	10 Area %	Fac Area %	Freq pps
S ABD DIG MIN (UL) - distal									
	4,6	-2,2	-1,3	100	12,8	-4	-9,2	100	3
	4,5	3,8	2,9	96,7	12,3	-4,9	-1,5	96,1	5
	4,4	-9,7	-4,8	94,7	12,9	-24,2	-16,1	100	10
	4,3	**20**	23,2	92,9	13,0	-26	-21,9	101	20
	4,3	**19,2**	**23,7**	93,2	12,3	-21,1	-24,9	96,2	20
	4,8	**24,7**	**27,7**	103	15,1	-12,3	-29,5	118	20
S NASALIS - facial									
	1,7	-0,7	-3,9	100	8,2	-2,5	-6,4	100	3
	1,7	-2,3	6,1	97,9	7,6	-10,2	-2,1	93,4	5
	1,5	**16,7(??)**	31	88,4	7,3	-10,2	166	89,3	10
	1,6	8,3	7,3	92,3	7,9	-15	-11,9	96,4	10

Repetitive nerve stimulation table

Conclusion: Our case shows that pembrolizumab might be associated with Lambert-Eaton myasthenic syndrome, the optimal treatment of which is still unclear; therefore, further studies are warranted.

Disclosure: Nothing to disclose.

Neuroimaging 1

EPO-328

Neurosonographic features of TORCH induced encephalopathy in newborns

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Background and aims: In all countries, the number of women that can be the reason of intrauterine infection of the fetus is increasing every year. In this regard, intrauterine infection among newborn babies is becoming more widespread. According to the literature from two to 60% of newborns are CMV infected and 10% of them are born with acute infection

Methods: Survey of 60 newborn was conducted – full-term ones – 33, preterm – 27 with neurosonographic imaging with the assessment of CNS in newborns depending on the type of infection

Results: Neurosonographic changes in patients with TORCH induced encephalopathy exhibit a high frequency of ischemic brain injury – in 64.4%, and intraventricular hemorrhage of varying severity – in 57.5%, and most pronounced in patients with combined infection. Multiple calcifications and cysts of the brain, as an outcome of intrauterine infection, occurred with similar frequency in all groups of infants with IUI and identified in 52.5% cases.

Conclusion: Thus, the acute process of IUI resulted in the development of polymorphic pathology of newborns, which was more common and severe in premature infants with mixed cytomegalovirus, herpes infection. This method is widely used in neonatology and perinatology research for the diagnosis of fetal and indirect confirmation of the presence of IUI.

Disclosure: Nothing to disclose.

EPO-329

Hemo- and cerebrospinal fluid dynamics changes in patients with “overcrowded posterior cranial fossa” syndrome using MRI

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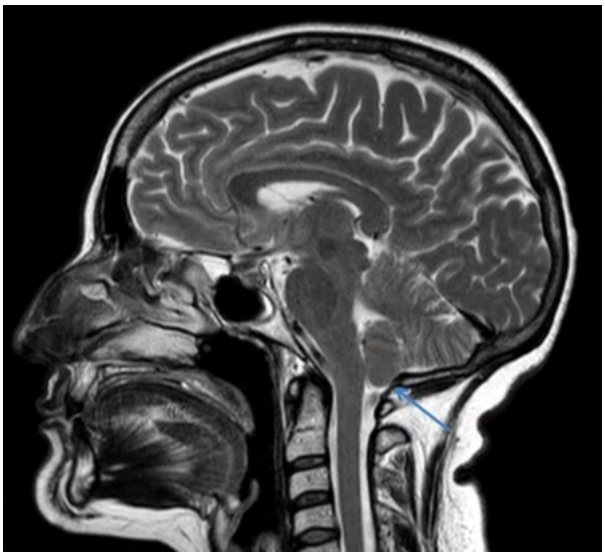
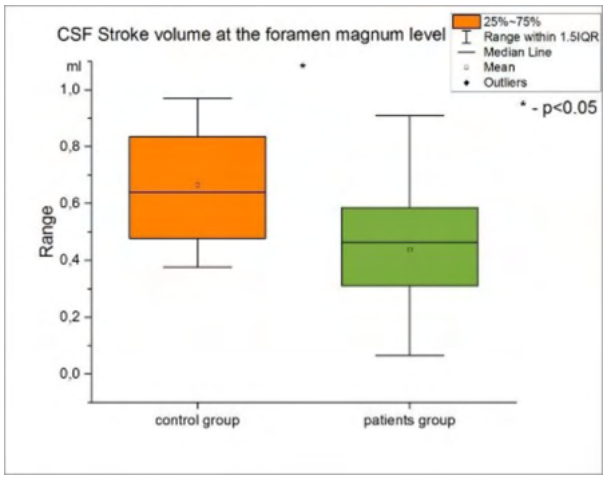
Background and aims: Using phase-contrast MRI to reveal a hemo- and cerebrospinal fluid dynamics changes in patients with “overcrowded posterior cranial fossa” syndrome.

Methods: The study involved 15 control patients and nine patients with radiological signs of craniovertebral junction angle decrease, a cerebellar tonsils ectopia (on 3–6mm lower than the foramen magnum (FM) level), narrowing of cisterna magnum. All patients had such clinical signs as headaches and neck pain, visual disturbances without any organic lesions of the brain. Patients underwent routine and phase-contrast MRI on the 3.0T “Inginia” Philips. We observed velocity values of blood and CSF flows at the some intracranial and C2-C3 cervical levels. A Pulsatility Index (PI), Arterial-Venous Delay (AVD) and Intracranial Compliance were analyzed.



T2-WI in sagittal plane. Low location of the cerebellar tonsils and narrowing of the cisterna magna (blue arrow).

Results: Arterial blood flow rates did not significantly differ. There was a tendency to increased venous outflow along the straight sinus and to decrease along the superior sagittal sinus in the patient group. In patients group the CSF volume and flux velocity values of caudal flow were significantly lower, but the flux velocity values of the cranial flow were significantly higher than in control group at the level of FM (<0.05). AVD is two times higher ($p<0.05$) at intracranial level, PI is 22% higher ($p<0.05$) at the FM level than the same parameters in the control group.



CSF Stroke volume changes at the level of the foramen magnum in control subjects and patients with "overcrowded posterior cranial fossa" syndrome.

Conclusion: The data obtained indicate a significant influence of the anatomical features of the craniovertebral junction level and the posterior cranial fossa on disturbances in the movement of CSF flow.

Disclosure: We thank the Russian Science Foundation (project No. 19-75-20093).

EPO-330

Magnetic resonance imaging in the assessment of brain connectome in patients with chronic tension-type headache

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Background and aims: The determination of changes in functional connections is promising in forming a new view on the etiology and pathogenesis of tension-type headache (TTH) and makes it possible to develop effective treatment tactics for patients. The aim of the study was to asses changes in the connectome in patients with TTH before and after application of osteopathic correction.

Methods: 24 patients (cf. age 32±5.6 years) with TTH were examined. Functional resting-state MRI was performed on a 1.5 T MR tomograph at two time points, before and immediately after osteopathic manipulation, respectively. Statistical processing and evaluation of the results of neuroimaging studies was carried out using the software package CONN V. 18, which serves to determine the relationships between different parts of the brain, the structure of various rest networks and working functional networks. We used the method of analysis based on the selection of the zone of interest.

Results: According to the results of an intergroup statistical analysis (2-sample t-test), when comparing the functional connectivity of the brain at rest in the first and second time points, a weakening of the negative functional connection of the medial prefrontal cortex with the left upper parietal lobe was revealed ($p<0.005$).

Conclusion: The results of the study indicate that patients with TTH before and after the application of osteopathic manipulation have differences in the functional activity of the brain.

Disclosure: Nothing to disclose.

EPO-331

Revealing structural and clinical heterogeneity in the neuromyelitis optica spectrum with unsupervised machine learning

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Background and aims: The spectrum of neuromyelitis optica (NMOSD) comprises different phenotypes and serotypes. Understanding disease heterogeneity is fundamental for targeted treatment. We aimed to unravel differences among NMOSD patients using unsupervised machine learning.

Methods: MR images and clinical data were obtained from 140 patients with NMOSD (n=105, 88 aquaporin-4-IgG [AQP4]-positive and 17 AQP4-negative) or AQP4-negative NMOSD-like manifestations (n=35, 17 recurrent myelitis [RM] and 18 recurrent optic neuritis [RON]) and 151 healthy controls from two centers. CNS damage (brain, optic nerve [ON] and cervical cord) was assessed in terms of lesions, normalized volumes, and cortical thickness. We computed between-group differences with age-, sex- and site-adjusted linear models. Based on structural measures, we ran unsupervised clustering analysis among NMOSD/NMOSD-like patients.

Results: Except for RM, NMOSD and NMOSD-like patients had diffused cortical atrophy ($p<0.008$), which was worse in the cingulate (AQP4-positive NMOSD, $p=0.001$), parietal (AQP4-negative NMOSD, $p=0.008$) and occipital lobes (RON, $p=0.022$). AQP4-positive NMOSD had reduced normalized brain volume ($p<0.006$) and cervical cross-sectional area ($p=0.02$). AQP4-negative NMOSD and RON had ON atrophy ($p<0.03$), the latter with additional optic chiasm atrophy ($p<0.001$). Clustering analysis identified three groups of NMOSD/NMOSD-like patients, with similar ON and cord lesion volume/length, number of optic neuritis/myelitis and phenotypes. Cluster-1 included patients with higher brain lesion volume ($p<0.048$), cluster-2 included patients with worse ON and cord atrophy ($p<0.048$) and cluster-3 included patients with greater cortical atrophy, milder disability, and higher rate of oligoclonal bands ($p<0.037$).

Conclusion: The heterogeneity of NMOSD spectrum goes beyond clinical manifestations and serostatus, possibly mirroring different pathophysiological substrates.

Disclosure: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

EPO-332

Intra-and Inter-Rater Reliability of Ultrasonographic Measurements of the Median Nerve Cross-Sectional Area of Filipinos

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Background and aims: The primary objective was to assess the intra- and inter-rater reliability of novice and expert measurements of the cross-sectional area (CSA) of the median nerve (MN) at the carpal tunnel inlet (CTI) and carpal tunnel outlet (CTO) of Filipinos.

Methods: A medical student with no peripheral nerve ultrasonography experience (novice) obtained serial bilateral measurements of the MN CSA at the CTI and CTO, with a single SonoSite Edge ultrasound machine with a linear array transducer, musculoskeletal setting, and electronic caliper function over the course of four months. Measurements were compared with those of an expert with more than 25 years of ultrasonographic experience. The latter was considered the reference standard. Both the novice and expert were blinded to each other's measurements.

Results: The Kendall's Coefficients of Concordance of intra-rater reliability measurements of MN CSA at the Left CTI, Right CTI, Left CTO, and Right CTO were 0.906, 0.857, 0.920, and 0.8065 for the novice; and 0.846, 0.872, 0.905, and 0.905 for the expert, respectively ($p<0.0001$). The Kendall's Coefficients of Concordance of inter-rater reliability between novice and expert measurements of MN CSA at the Left CTI, Right CTI, Left CTO, and Right CTO were 0.878 ($p<0.01$), 0.822 ($p<0.01$), 0.595 ($p=0.193$), and 0.679 ($p=0.068$), respectively.

Conclusion: There were strong degrees of intra-rater reliabilities, and moderate to strong degrees of inter-rater reliabilities in novice and expert measurements of MN CSA using ultrasonography.

Disclosure: Nothing to disclose.

EPO-333

Imaging diagnosis of rare neurological complications in patient with lupus - a description of two cases

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Background and aims: Systemic lupus erythematosus (SLE) is an autoimmune disease that develops as a result of complex disorders of immune system. The aim of study is the radiological evaluation of the brain in two patients with lupus who developed neurological complications.
Methods: Two patients with lupus were enrolled in the study. 41 years old female was hospitalized due to headache, neck pain and deterioration of vision. The second case was a 37 year old patient hospitalized due to epileptic seizures. Patients were sent for neuroradiological investigation.
Results: In the first patient Doppler ultrasound showed thickening of the right vertebral artery wall in V1-V2 segments. Contrast-enhanced brain MRI confirmed wall thickening with segmental enhancement in the proximal V2 and distal V1 segment indicating inflammatory changes; angio-MR revealed narrowing of the vertebral artery lumen - vertebral artery inflammation was diagnosed. Brain MR of the second patient detected poorly delimited inflammatory lesions enhancing after contrast administration, localized in the medial part of the left temporal lobe and bilaterally next to the third ventricle. In angio-MR there were clearly visible irregularities in the diameter. Cerebral vasculitis was diagnosed. Control MR examination after treatment showed partial regression of the inflammatory changes and no post-contrast enhancement.
Conclusion: The neurological complications in patients with lupus include inflammation of the vertebral artery, encephalitis and vasculitis. MR examination is the method of choice in the diagnosis and monitoring this type of changes. Doppler ultrasound is an useful method in assessment of the carotid and vertebral arteries morphology in their extracranial sections.
Disclosure: Nothing to disclose.

EPO-334

Small posterior cranial fossa without cerebellar tonsils ectopia and without syringomyelia

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Background and aims: Clinical-MRI comparisons revealed the insufficient of using cerebellar tonsils herniation (TH) of 5mm or more as a single diagnostic criterion for Chiari malformation type 1 (CM1), and also proved the significance of congenital small posterior cranial fossa (PCF) in the pathogenesis of primary "classical" CM1 and its subtypes – CM0 and CM1.5. This, in turn, led to practical interest in the study of non-rubrified forms of classical CM1. The present study aimed to define the morphometric features of the small PCF without cerebellar ectopia and without syringomyelia ("CM0 without S") in clinically symptomatic patients.
Methods: MRI comparisons were performed between two groups of patients with CM1-like symptoms (30 subjects each): "CM0 without S" (small PCF, TH <2mm), CM1 (small PCF, TH≥5 mm), and control group.
Results: Both groups of patients significantly differed from the control in 29 identical MRI parameters, which indicated a decrease in height, flattening and overflow of PCF. The combination of reduced size of the foramen magnum area with increased length of perpendicular between a line connecting the basion and the inferoposterior edge of the C2 to the ventral dural was unique characteristic of "CM0 without S". This may explain the absence of TH in this group of patients with small PCF.
Conclusion: The results of the study suggest the possibility of including symptomatic form of "CM0 without S" in the spectrum of CM1-like pathology as a distinct subtype.
Disclosure: No conflict of interest.

EPO-335

Medial longitudinal fasciculus: round up the usual suspects!

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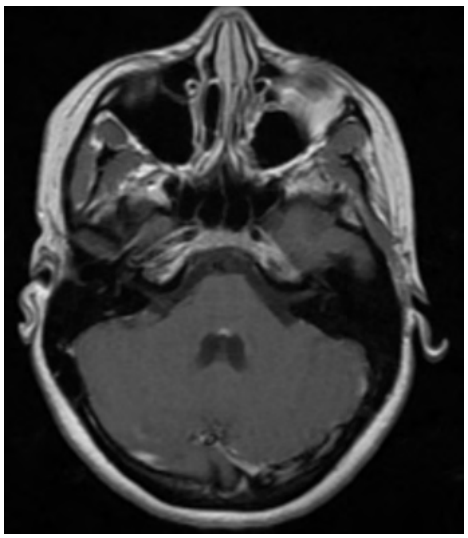
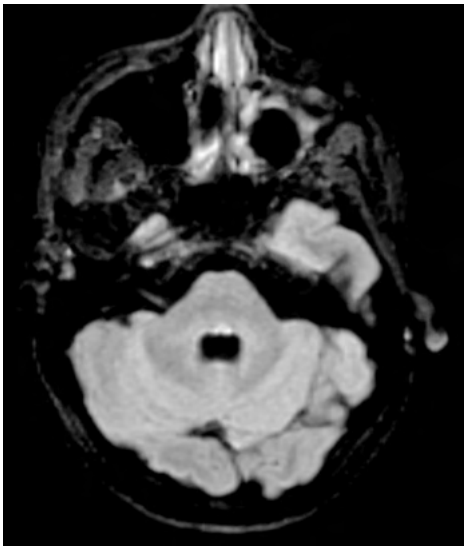
Background and aims: We describe the physiopathology, semiology and etiology of medial longitudinal fascicle (MLF) lesions regarding a clinical case.
Methods: We present the case of a 28-year-old woman admitted to the neurology ward for subacute onset blurred vision and dizziness in the previous days. Upon arrival, the patient presented isolated bilateral internuclear ophthalmoplegia (INO).
Results: A wide range of tests were carried out, of which the most relevant was the MRI. A selective hyperintensity in fluid-attenuated inversion recovery (FLAIR) sequences in the MLF was observed in the pons, with active contrast enhancement. The MRI showed also multiple hyperintense white matter lesions in FLAIR sequences, only some of them with contrast enhancement. After administering methylprednisolone one gram every 24 hours for five days, the patient presented only subtle horizontal dissociated nystagmus in dextroversion and was discharged. At the time, the patient met McDonald's criteria for relapsing remitting multiple sclerosis.



T1 with gadolinum sequence, that shows bilateral enhancement of MLF



FLAIR sequence that shows bilateral hyperintensity of MLF

Conclusion: The MLF connects the sixth cranial nerve to the subnucleus of the medial rectus muscle within the nucleus of the third cranial nerve, as well as vestibular pathways that enable the horizontal, vertical and torsional vestibulo-ocular reflexes. Its selective involvement explains all of the symptoms of this patient. Reviewing the literature, unilateral involvement is more frequently of ischemic origin and bilateral involvement, as our patient showed, eminently demyelinating. Within the demyelinating diseases spectrum, multiple sclerosis is the most frequent cause of MLF involvement.
Disclosure: Nothing to disclose.

Sleep disorders

EPO-336

Prevalence of sleep disturbances in Parkinson's disease patients during the COVID-19 lockdown in Romania

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Background and aims: Patients diagnosed with Parkinson's disease (PD) may experience a broad spectrum of sleep disturbances. COVID-19 pandemic and the restrictive measures that were imposed have impacted several aspects of life, including sleep. Objectives: To identify the prevalence of various sleep disorders among PD patients in Romania during the national lockdown period imposed in the context of COVID-19 pandemic.
Methods: Prospective online survey on 134 PD patients from the whole Romania. The online survey included items regarding socio-demographic data, various questions related to sleep disorders and the way these sleep disturbances changed during the quarantine period during 16th March – 14th May 2020.
Results: There were 74 men (55%), mean age 61.3±5.42 years [range 56–67 years]. Most patients reported at least one sleep disturbances, the most prevalent symptom being insomnia (79.85%), followed by frequent nighttime awakenings (68.65%). The most common sleep complaints that were aggravated during lockdown comparing to baseline were unrefreshing sleep (50.7%), frequent awakenings (19.4%), and sleep initiation difficulties (17.9%). Among the new-onset symptoms occurring during the quarantine, sleep initiation difficulties and early awakenings were the ost commonly reported. The majority of the patients (69.4%) noticed a reduction of the total sleep time during the lockdown.
Conclusion: Conclusions: sleep disorders are common in PD patients and most of the sleep-related complaints were aggravated during the lockdown measures.
Disclosure: Nothing to disclose.

EPO-337

Risk-taking propensity in narcolepsy with cataplexy

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Background and aims: Narcolepsy with cataplexy (NC) is caused by the loss of hypothalamus neurons that produce hypocretin (Mahoney et al., 2019). Hypocretin activity is associated with reward processing and addiction through projections to dopaminergic regions (Baimel et al., 2017), with consequences on decision-making (Bayard et al., 2011). Moreover, excessive daytime sleepiness (EDS) could influence the performances in tasks related to this executive function (Aidmar et al., 2019). The aim of our study was to compare NC patients and controls regarding risk-taking propensity.
Methods: 15 drug-free patients with NC (male: 53.5%; mean age=47.20 yrs, SD=17.95 yrs) were compared with healthy controls. All NC patients underwent one night of polysomnography followed by a multiple sleep latency test. All participants were administered the Balloon Analog Risk Task (BART) and Go/NoGo task.
Results: Mann-Whitney U test indicated that Go/NoGo Reaction Time was significantly greater for healthy controls (Mdn=1,039.25 ms, SD=146.22 ms) than for patients (Mdn=588.57 ms, SD=422.68 ms), U=40.00, rp-b=0.64, $p < 0.01$ and that BART Mean Blue Adjusted was smaller for healthy controls (Mdn=12.48, SD=7.95) than narcoleptic patients (Mdn=15.60, SD=10.24), U=80.00, rp-b=0.29, $p > 0.15$).
Conclusion: Our study showed that NC patients have higher risk-taking propensity and lower reaction time on sustained attention and inhibitory control task. Further studies should focus on other factors that could affect cognitive performances in NC patients to understand the cause of the executive deficit in NC patients. Moreover, the evaluation of patient in other EDS categories (i.e., idiopathic hypersomnia) is mandatory.
Disclosure: Nothing to disclose.

EPO-338

Hypersomnia secondary to Hashimoto encephalitis

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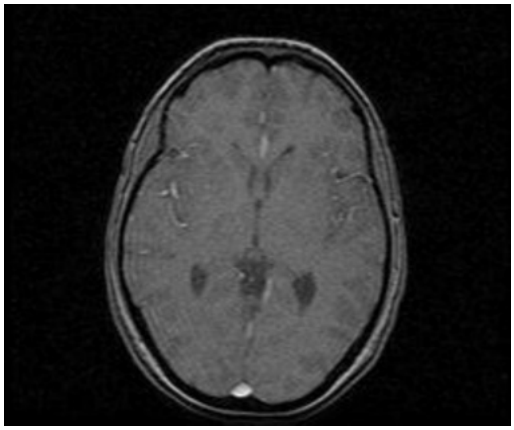
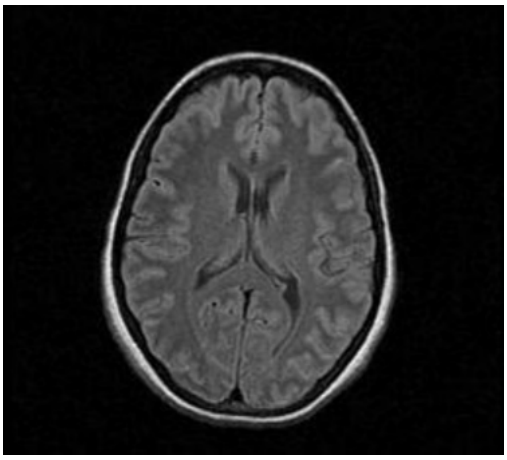
Background and aims: Chronic hypersomnias secondary to structural pathology of the central nervous system are not frequent. They have been related to cerebral vascular disease, tumors, trauma, or viral encephalitis. However, cases of hypersomnia secondary to encephalitis of autoimmune origin are exceptional.
Methods: We present a clinical case of diurnal hypersomnia secondary to Hashimoto's encephalitis with evolutionary follow-up over 10 years.
Results: A 32-year-old woman, with a history of unknown hypothyroidism, admitted to the ICU with Glasgow 8 and sphincter relaxation. Neuroimaging tests, CSF study, blood analysis and urine toxins were performed, without observing significant alterations. In several EEGs a pattern of non-convulsive status epilepticus was observed, this being resolved with antiepileptic drugs. Empirical treatment with antibiotics and antivirals was started and, due to the suspicion of autoimmune encephalitis, high-dose corticosteroids were started with great clinical and electrical improvement. Immunity study was requested, with negative onconeuronal antibodies and elevated anti-peroxidase antibodies (451), for which Hashimoto's encephalitis was diagnosed. After entering work life, the patient reported excessive daytime hypersomnia despite good night's rest (Epworth Test 15/24). The polysomnography was normal and the multiple sleep latency test showed pathological hypersomnolence (mean sleep latency: 5.5). During 10 years of follow-up, several therapeutic trials have been conducted (bupropion, methylphenidate, reboxetine, fluoxetine …), achieving a greater clinical response with bupropion.



MRI with contrast without pathological findings



MRI flair sequence without pathological finding

Conclusion: Despite the low incidence of long-term sequelae of Hashimoto's encephalitis, our patient developed persistent hypersomnolence. Therefore, we must not forget the possibility of the appearance of these secondary clinical consequences in patients with this disease.
Disclosure: I have not received commercial or institutional support.

EPO-339

Revalence of sleep disturbances and the role of flashbacks among military servicemen after acute stress related to war

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Background and aims: Sleep disturbances are prevalent among military personnel with war-related acute stress. Our study aimed to determine the prevalence of sleep disturbances and their relationship to flashbacks among servicemen after the recent war in Artsakh.
Methods: We involved Armenian servicemen without severe physical injury recovering at a specialized facility. We used the validated Armenian version of Pittsburgh Sleep Quality Index (PSQI-Arm) and recorded the presence of the following symptoms: insomnia and its phenotypes: sleep-maintenance insomnia (SMI), sleep-onset insomnia (SOI), abnormal circadian rhythm (ACR), nightmares, excessive daytime sleepiness (EDS), flashbacks.
Results: Overall 66 servicemen with mean age 19 (18–37) participated in our study. According to PSQI-Arm results, 95.45% of participants had poor sleep quality. The reported mean sleep latency was 115.3 minutes (5–480) and the average total sleep time was 5.8 hours. The prevalence of ACR (60.6%) and nightmares (0.8%) also was high in contrast to EDS (21.2%). Of all participants 54.55% had flashbacks, and 90.9% of participants had insomnia (SOI-83.1% and SMI-32.31%), 80% of those with flashbacks had higher insomnia (p=0.004). Moreover, servicemen with flashbacks were more likely to have SOI (94.3%, p=0.009) not SMI. We found no connection of nightmares, ACR, and EDS to the presence of flashbacks (p>0.05).
Conclusion: Our study results show that sleep disorders are common in the post-war population. Military servicemen had a high prevalence of sleep complaints, short sleep duration, and flashbacks, the latter more likely to have SOI rather than SMI.
Disclosure: Nothing to disclose.

EPO-340

The impact of restless legs syndrome on health-related quality of life in epilepsy

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Background and aims: Restless legs syndrome (RLS) is a sleep-related movement disorder characterized by unexplained urge to move limbs, mostly due to unpleasant sensations/paraesthesias, which worsen at rest and usually occur at bedtime. RLS prevalence is higher in patients with epilepsy (PWE) than in general population. Epilepsy has an impact on physical, mental and social aspects of patients' lives. RLS may be an important factor affecting health-related quality of life (HRQOL) in PWE. We aimed to study the influence of RLS on HRQOL in PWE.
Methods: Our study involved PWE admitted to tertiary sleep and epilepsy centres. The RLS diagnosis was placed according to IRLSSG criteria. HRQOL was assessed quantitatively by SF-36 self-administered generic instrument consisting of eight domains: D1 – Physical Functioning, D2 – Physical Role-Limitations, D3 – Role-Limitations Due to Emotional Problems, D4 – Energy/Fatigue, D5 – Emotional Well-Being, D6 – Social Functioning, D7 – Pain, D8 – General Health.
Results: We enrolled 175 PWE (mean age-35.4; F/M-47.4%/52.6%). PWE with RLS (RLS group-RG) comprised 20.6% of the study population (mean age-42.6). PWE without RLS (no RLS group-NRG) were younger (mean age-33.6, p<0.01). RG reported lower HRQOL compared to NRG. Mean values for each SF-36 domain are presented for RG/NRG respectively: D1-59.5/70.6 (p<0.05), D2-23.4/45.6 (p<0.05), D3-30.2/45.8 (p>0.05), D4-41.4/55.1 (p<0.05), D5-46.1/54.8 (p>0.05), D6-51.6/65.8 (p<0.05), D7-53.8/66.9 (p<0.05), D8-42.5/49.7 (p>0.05).
Conclusion: PWE with RLS report worse HRQOL, especially for physical domains. PWE with RLS were older. In order to improve management of PWE, the impact of RLS on HRQOL should be addressed by physicians.
Disclosure: Nothing to disclose.

EPO-341

Prevalence and impact of restless legs syndrome during COVID-19-related restrictive measures in Armenia

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Background and aims: COVID-19 led to State of Emergency (SE) in Armenia (March 2020). Restless legs syndrome (RLS) is characterized by an urge to move limbs, which mostly occurs at bedtime and during inactivity. Low activity may lead to RLS exacerbation during lockdown. **Aim:** to evaluate RLS prevalence in adults before and during SE (BSE, DSE), and its impact on affective symptoms (AS) and sleep quality (SQ).
Methods: Social media users were anonymously assessed by online questionnaire. It covered sleep-related habits, subjective sleep complaints, and affective symptoms, divided into two parts: BSE and DSE. RLS-DSE was confirmed by the first four international criteria (4+), while for RLS-BSE we used a single question confirming the presence of RLS before. We assessed RLS days per week (d/w), and five SQ categories from "very good" to "very bad".
Results: The participants (n=499, mean age-30.3, females-89%) had the following RLS-BSE/RLS-DSE distribution: 13.3%/42.4%. Only 4% RLS-DSE corresponded to four international criteria. During SE, 90.4% of RLS-BSE remained with symptoms. Interestingly, in those with no RLS before SE, 37% developed RLS symptoms de novo, of which 2.3% being de novo 4+ RLS. RLS participants: had 4.75 d/w with symptoms, positively correlating with poor SQ ($r=0.262$, $p<0.001$); reported more AS: mood disturbances – 0%/4.91% ($p<0.05$); anxiety-2.3%/4.62% ($p>0.05$); and had more d/w with AS: depression-2.57/3.65 ($p<0.03$); anxiety-2.3/3.3 ($p<0.03$).
Conclusion: RLS symptoms were prevalent among people in self-isolation. De novo RLS was reported. Those with RLS symptoms had mostly severe course defined by days per week. RLS was associated with poorer SQ and worse AS.
Disclosure: Nothing to disclose.

EPO-342

Children with sleep disordered breathing have a risk for development of specific deficit in memory

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Background and aims: It is known that sleep disordered breathing (SDB) in children is a risk for development of deficit in executive abilities. However, we need to do further research for revealing specific relationship between SDB and deficit in executive abilities. The goal of this research was to examine the hypothesis that children with SDB have a deficit in memory in delayed recall condition.
Methods: The experimental group included 18 children with SDB (mean age 6.12±1.32 years, 13 boys and five girls). The control group included 18 typically developing children. The children from experimental and control group were matched for gender and age. Children from both groups were assessed with Memory for Names subtest from NEPSY. This subtest is designed to assess the ability to learn and recall the names in immediate and delayed recall conditions. ANOVA with repeated measures was used to reveal group differences in reproducing the names in immediate and delayed recall conditions.
Results: We have not revealed significant differences ($p=0.05$) between children from experimental and control group in reproducing the names in immediate condition. However, the interaction of condition type and group was significant [$F(1,32)=10,56$]. Children with SDB were less successful in reproducing the names in delayed recall condition in comparison to children from control group.
Conclusion: In view of the obtained results it can be assumed that sleep disordered breathing is a risk for development of the specific (not global) deficit in executive abilities. However, we need to do further research to confirm this hypothesis.
Disclosure: Nothing to disclose.

EPO-343

Mapping Insomnia and Circadian Preference to Mental Health across the Lifespan and Sexes

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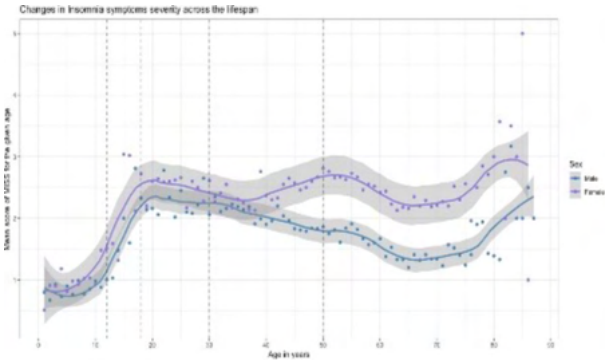
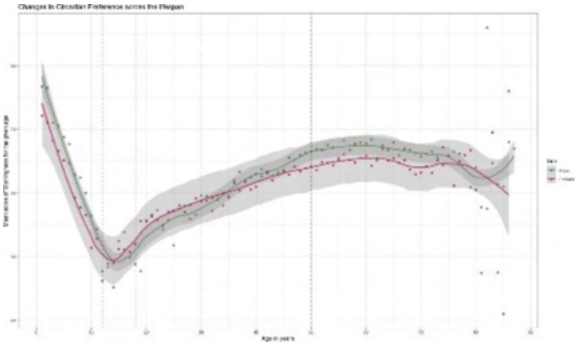
Background and aims: Insomnia and delayed circadian rhythm are associated with different psychiatric disorders. Mapping overlap and differences of distinct sleep profiles across different types of psychiatric problems in men and women across the lifespan may aid diagnostics, prevention and treatment of psychiatric disorders.
Methods: We use cross-sectional survey data from 37,716 Dutch individuals aged 4–91, a subsample from the Lifelines cohort. We will identify subgroups of persons who cluster according to their insomnia symptoms and circadian preferences via latent class analysis. For each age/sex stratum, sleep profiles will be linked to different dimensions of psychopathology (attention deficit hyperactivity disorder, autism, aggression, depression, anxiety, substance use) using analysis of covariance. Analyses were pre-registered on Open Science Framework (osf.io/FM4B3).
Results: Preliminary findings show mostly morning preferences in childhood, evening tendencies in adolescence and intermediate in adulthood. Higher insomnia was related to higher eveningness ($r=-0.29$, $p<0.001$). Insomnia increases with age, more so for females than for males. Men have clinical insomnia more often than women in young adulthood (OR=8, $p<0.05$) but the opposite holds in middle adulthood (OR=0.4, $p<0.05$). We identified three specific patterns of circadian preferences and insomnia symptoms comparable among all age/sex strata. These sleep profiles will be linked to the different psychological dimensions, which will be elucidated during the talk.



Changes in insomnia across the lifespan in men and women



Changes in circadian rhythm across the lifespan in men and women

Conclusion: Individuals in the general population can be classified according to their circadian preference and insomnia symptoms. Such sleep profiles likely have unique associations to distinct dimensions of psychopathology, which has implications for diagnosis, prevention and treatment of both sleep and mental disorders.
Disclosure: The authors report no conflicts of interest.

EPO-344

Pathogenetically grounded methods of diagnosis and treatment of bruxism

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Background and aims: The aim of the study was investigation the levels of anxiety, depression, determination of blood serum serotonin concentration and complex treatment of increased abrasion of hard tissue of teeth of patients with bruxism.
Methods: Materials and methods. The study involved 157 patients who complained of pain and discomfort in the masticatory muscles, changing the face shape, abrasion of hard dental tissues, petulance. Patients underwent a neurological and dental status study, masticatory muscles electromyography (EMG), determination of anxiety and depression level (HADS) and the concentration of blood serum serotonin by enzyme-linked immunosorbent assay using Serotonin ELISA kits. To relieve masticatory muscles hypertonicity the botulinum therapy was carried out.
Results: Results. Before treatment all patients had hypertonicity of the masticatory muscles accompanied by pain (4.0 (2.0; 6.2) VAS), a diagnosis of Bruxism (F45.8), increased abrasion of hard dental tissues (k03.0). The level of anxiety and depression (31,0 (30,0; 40,0) and 9,0 (8,0; 14,0) respectively, HADS). The serum serotonin level –149.8 (123.0; 160.5) ng /ml when normal (227.1 (199.6; 264.8) ng /ml). After botulinum toxin type A treatment a decreasing of the masticatory muscles tone, pain 2.0 (1.0; 3.0), a degree of anxiety and depression 28,0 (27,0; 33,0) 7,0 (5,0; 9,0) points were revealed. The concentration of serotonin became 183,5 (169,0; 201,0) ng / ml.
Conclusion: Conclusion. Determination of the blood serum serotonin concentration an serve as a method for early diagnosis of bruxism (RF patent for invention No. 2 633 753 - 17.10.2017).
Disclosure: Nothing to disclose.

Ageing and dementia 3

EPO-345

Acute stroke pathway intervention results in a secondary care centre during the COVID-19 pandemic

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Background and aims: The COVID-19 pandemic changed how we manage acute stroke, due to safety concerns and resource redestribution. We aimed: to compare NIHSS and modified Rankin scale (mRs) on discharge with admission NIHSS and pre-stroke mRs, respectively; to compare NIHSS and mRs scores on discharge between the intervention (thrombolysis and/or thrombectomy) and the no-intervention group.

Methods: Prospective cohort study conducted at a Neurology department of a secondary care centre, between 15th march and 11th september 2020. We included consecutive acute stroke admissions and excluded non-vascular etiologies. Summary measures are presented as N(%) ou median(interquartile range), unless indicated otherwise. Mann-Whitney-U and Wilcoxon tests were performed, assuming statistical significance for p<0.05 (IBM SPSS Statistics 24).

Results: We included 81(93%) acute ischemic strokes – 45(55,6%) males, aged 74(21.0) years. The intervention group's (n=36) discharge NIHSS was significantly lower than the admission NIHSS [respectively, 5,5(8,0) and 13,89(7,0) – average(standard deviation); p=0,025] and comparable in the no-intervention group (n=42) [1(8,0) and 3(6,0)], respectively; p=0,160]. The discharge mRs was significantly higher than the pre-stroke mRs in both groups [intervention group 3,5(2,75) and 0(0,0), respectively, p<0,001; no-intervention group 2(3,5) and 0(0,0) respectively, p<0,001]. The intervention group's admission NIHSS was significantly higher than the no-intervention group's [13,9(7,0) and 3(6,0) – average(standard deviation); p<0,001], as were the discharge NIHSS [5,5(8,0) and 1(8,0); p=0,002] and discharge mRs [3,5(2,8) and 2(2,5); p=0,002], respectively.

Table 1. Interventions in acute ischemic strokes

Characteristics	Intervention type[a] IV Thrombolysis	Thrombectomy
Acute treatment - N (%)[b]	25 (30,9)	19 (23,5)
Time from admission to treatment (minutes) - median (IQR)	57 (47,0)	242 (104,0)
Time from onset to treatment (minutes) - median (IQR)	176,2 (53,8)[c]	334 (161,0)
TICI 0		2 (13,3)
2b		9 (60,0)
3		2 (13,3)
Recanalização espontânea		2 (13,3)

IQR – interquartile range; IV – intravenous; N – number; TICI - *Thrombolysis in cerebral infarction*
[a]8 patients underwent both treatments
[b]Percentage of acute ischemic strokes that underwent thrombolysis or thrombectomy, respectively
[c]Average (standard deviation)

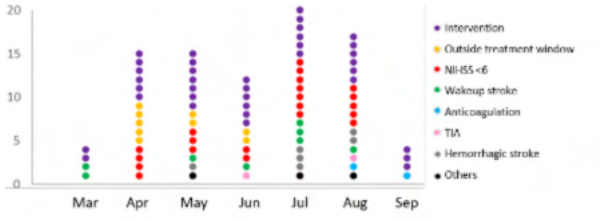
Number of acute ischemic strokes submitted to acute intervention, time

Table 2. Acute ischemic stroke outcomes

Characteristics	NIHSS Admission	Discharge	p[a]	mRs Pre-stroke	Discharge	p[a]
Acute interventions						
Yes - median [IQR]	13,89 (7,0)[b]	5,5 [8,0]	**0,025**	0 [0,0]	3,5 (2,75)	**<0,001**
No - median [IQR]	3 (6,0)	1 [8,0]	0,160	0 [0,0]	2 [3,50]	**<0,001**

IQR – interquartile range; NIHSS – National Institutes of Health Stroke Scale; mRs – modified Rankin scale
[a]Statistical significance for p value <0,05
[b]Average (standard deviation)

Comparison of NIHSS and modified Rankin scale (mRs) on discharge with admission NIHSS and pre-stroke mRs scores, respectively, in the intervention and no-intervention groups.



Dotplot: number of strokes submitted to acute intervention and number of strokes excluded from acute intervention (and the reason why).

Conclusion: The intervention group presented clinical improvement. Nonetheless, both groups kept significant functional impairment on discharge. Concerning the no-intervention group, delayed ward admission and, consequently, delayed motor rehabilitation may have been responsible.

Disclosure: I declare that this research didn't receive commercial or institutional support of any kind.

EPO-346

The effectiveness of pharmacist-led medication reviews in people living with dementia: a systematic review.

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Background and aims: People living with dementia (PwD) are at risk of experiencing drug-related problems; higher levels of comorbidities and other concerns unique to PwD, increase their risk. The medication review (MR) is defined as the systematic evaluation of a person's medicines, with the aim of optimising outcomes. We propose that a pharmacist led MR (PMR) could be an effective tool to reduce drug-related problems; thus, resulting in reduction of hospital readmissions, emergency department (ED) re-presentations and improve QoL.
Methods: The primary aim was to evaluate the effectiveness of PMR on the hospital readmissions or ED re-presentations of PwD. The secondary aim was to evaluate the impact of PMR on QoL of PwD. Randomised controlled and quasi-controlled trials were included. Electronic searches were undertaken in AMED, CINAHL, Embase and Medline databases.

Author (Year)	Study Design and Country	Study Setting and Conditions	Participants Groups	Medication Review (MR) and other Intervention Details	Outcome Details	Comments
Sakakibara et al. (2015)	Quasi Randomised Controlled Trial Australia	Clinic Dementia	≥65 years Intervention: 19 Control: 13	Medication review with the aim of prescription reduction	QoL was maintained in the intervention group	QoL in the control group only decreased slightly
Kable et al. (2020)	Quasi-controlled trials	Hospital Dementia	Intervention 290 Control: 236 >50years -Mean age 84±years	Medication reconciliation on admission and discharge Medication review patient/ carer counselling on use of medication dose administration aids Provision of the discharge medication list and medication counselling Nurse-led care assessment	No effect of on the re-presentations to the Emergency department and readmissions of the intervention group at 3 months	
				Informing GP of discharge medication and any changes. Recommendation of GP to organise home medicine review by community pharmacist.		
Gustafsson et al. (2017)	Randomised Controlled Trial Sweden	Hospital Dementia or cognitive impairment	Intervention 230 Control: 230 ≥65 years	Medication reconciliation Medication review Participation in ward rounds	No significant improvement in drug-related readmission in PwD at180 days No significant improvement in drug-related readmission in PwD at 30 days Significant reduction in drug-related readmissions at180 days in intervention group among	

Characteristics of included studies

Results: Of the 6,759 studies from the original search, ten were reviewed as full text, and three studies were included. Two studies could not identify a reduction in hospital readmissions (all-cause and drug-related) and ED re-presentations after PMR; however, one of these studies showed a reduction in drug-related readmissions in PwD without heart failure and in a post-hoc analysis. The final study showed QoL was only maintained in the intervention group receiving MR, but not in the control group.
Conclusion: There was very low certainty of evidence that PMR reduced the rate of admissions or ED re-presentations in PwD. However, some evidence suggested stabilisation of QoL. Further well-designed studies are needed to assess the effectiveness of PMR in PwD.
Disclosure: Nothing to disclose.

EPO-347

I stay at home with headache. A survey to investigate the effects of lockdown on headache in Italian children

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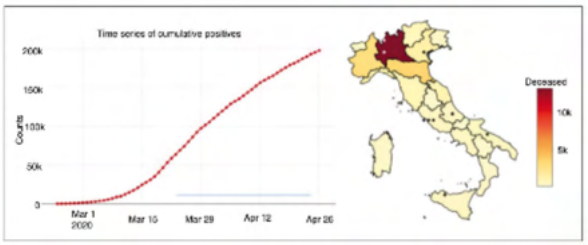
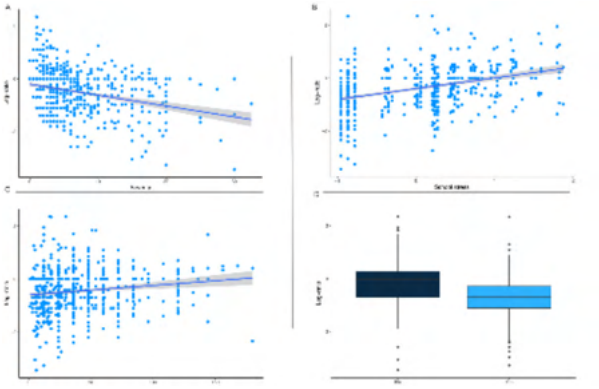
Background and aims: The present Italian multicenter study aimed at investigating whether the course of primary headache disorders in children and adolescents was changed during the lockdown necessary to contain the COVID-19 emergency in Italy.



(a) Trend of infections for COVID-19 in Italy during the period of submission of questionnaire (blue line). (b) Geographical distribution of deaths for COVID-19. Asterisks show the locations of the headache centers participating in the study.

Methods: During the lockdown, we submitted an online questionnaire to patients already diagnosed with primary headache disorders. Questions explored the course of headache, daily habits, psychological factors related to COVID- 19, general mood and school stress. Answers were transformed into data for statistical analysis. Through a bivariate analysis, the main variables affecting the subjective trend of headache, and intensity and frequency of the attacks were selected. The significant variables were then used for the multivariate analysis.

Results: We collected the answers of 707 patients. In the multivariate analysis, we found that reduction of school effort and anxiety was the main factor explaining the improvement in the subjective trend of headache and the intensity and frequency of the attacks ($p<0.001$). The greater the severity of headache, the larger was the clinical improvement ($p<0.001$). Disease duration was negatively associated with the improvement ($p<0.001$). It is noteworthy that clinical improvement was independent of prophylaxis ($p>0.05$), presence of chronic headache disorders ($p>0.05$) and geo- graphical area ($p>0.05$).



Results from multivariate analysis. Relations between frequency log ratio and severity score (a), duration of headache in months (b), school anxiety (c) and reduction of school effort (d).

Conclusions: Our study showed that lifestyle modification represents the main factor impacting the course of primary headache disorders in children and adolescents. In particular, reduction in school-related stress during the lockdown was the main factor explaining the general headache improvement in our population.

Disclosure: Nothing to disclose.

EPO-348

Motor Impairment in MS: Analysis from the North American Registry for Care and Research in Multiple Sclerosis (NARCRMS)

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Background and aims: Expanded Disability Status Scale (EDSS) and upper and lower limb motor performance metrics are routinely collected in NARCRMS participants.
Methods: Compare and correlate upper and lower extremity motor function in NARCRMS participants at enrollment. Current enrollment is 816 patients from 25 sites in the United States and Canada. 674 patients with complete information on EDSS and lower (25-foot time walk) and upper [9-hole peg (9-HP) test] limb motor function contributed to this study.
Results: A mean 25-foot walking speed of 4.9 seconds was recorded in patients with EDSS 0 with progressive decline (5.6 and 8.2 seconds at EDSS 3.0 and 4.0 respectively) to 18.1 seconds at EDSS 6.5 (Table 1). For upper limb function, patients with EDSS 0 had a mean 9-HP test speed of 20.1 seconds in dominant (D) and 21.1 seconds in non-dominant (ND) hands, with decline starting at EDSS 2.5 (24.5 and 23.6 seconds for D and ND hands respectively) progressing to 36.0 and 50.9 seconds for the D and ND hands at EDSS 6.5 (Table 2).

Average 25 Foot Walk by EDSS (n=677)		
EDSS	# Subjects	25 Foot Walk (seconds)
0	112	4.9
1	106	4.7
1.5	137	5.2
2	130	5.2
2.5	49	5.4
3	42	5.6
3.5	29	6.6
4	29	8.2
4.5	7	8.6
5	5	7.9
5.5	4	9.8
6	16	8.6
6.5	11	18.1

Table 1: Average 25 Foot Walk by EDSS

Average 9 Hole Peg Test by EDSS (n=674)			
EDSS	# Subjects	9 HP Dominant (seconds)	9 HP Non-Dominant (seconds)
0	109	20.1	21.1
1	106	20.1	21.3
1.5	139	20.6	21.9
2	125	21.8	22.7
2.5	48	24.5	23.6
3	41	23.5	25.4
3.5	29	23.8	23.8
4	30	25.8	26.2
4.5	7	27.6	29.1
5	5	28.5	28.4
5.5	4	29.8	30.4
6	15	35.6	31.1
6.5	16	36.0	50.9

Table 2: Average 9 Hole Peg Test by EDSS

Conclusion: Correlation of 25-foot walking speed to EDSS scale reiterated EDSS is a "walking scale". Decline in hand function beginning at EDSS 2.5 was unexpected as it is generally thought to be less affected in early MS. Progressive decline of hand function with EDSS confirms 9-HP test as a good measure of declining hand function and should be included in clinical monitoring.
Disclosure: NARCRMS receives funding from the CMSC and several industry partners.

EPO-349

Intention to be force efficient improves high-level object control differentially in young and elderly adults

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Background and aims: Successful object manipulation requires anticipatory high-level-control of finger positions and forces to prevent object slip and -tilt. Previous studies showed that cognitive motor control and grip force economy declines with aging.

Methods: Here, we theoretically show how grip force economy depends on the modulation of the centers of pressure on opposing grip surfaces (deltaCoP) according to object properties. In a grasp-to-lift study with young and elderly participants we investigated how the instruction to lift the object with efficient GF influences the anticipation of torques, deltaCoP and GF control during complex variations of mass distributions and surface properties.

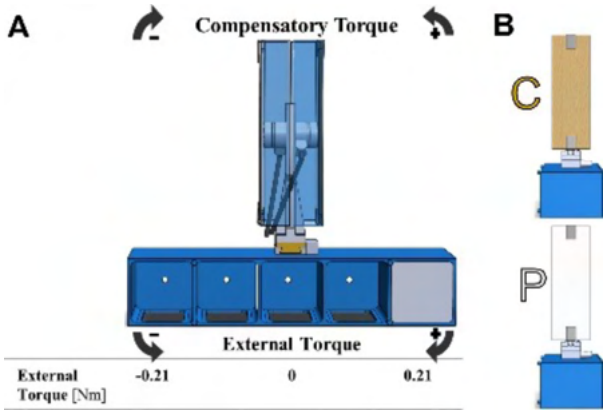

Figure 1: Apparatus and Experimental Procedures. (A) The custom-built grip-device consists of a handle element mounted centrally on a horizontal bar (frontal view). The handle element allowed subjects to freely choose digit placement on the grip surfaces

Results: Provision of the explicit instruction to strive for force efficiency prompted both age groups to optimize their deltaCoP modulation - although to a lesser degree in the elderly - and also led to a refinement of torque anticipation for a right-sided weight distribution in the young- but not the elderly participants. Consequently, marked drops in GF levels resulted. Furthermore, participants enhanced CoP modulation and lowered GF safety ratios in challenging surface conditions. Higher GF in the elderly reflected decreased skin-surface friction. However, we found no evidence for an increase of GF excess due to deficient deltaCoP modulation or increased safety margins in the elderly suggesting preserved neural control.

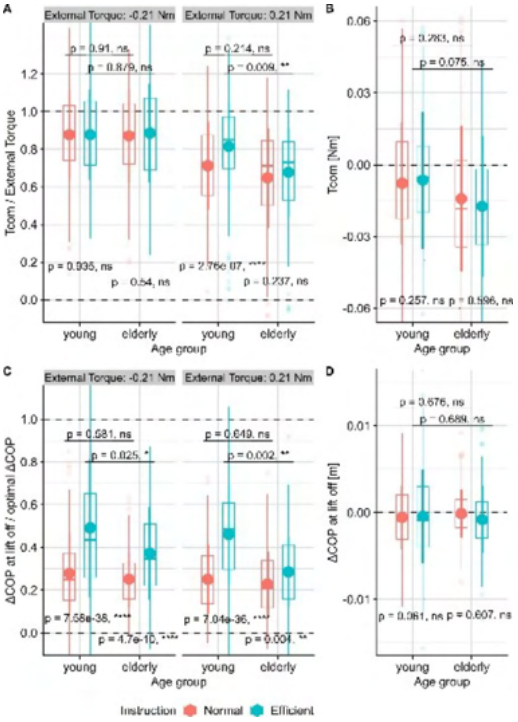

Figure 2: Tcom and COP anticipation for trials 3–6 per external torque. T_com/(External Torque)

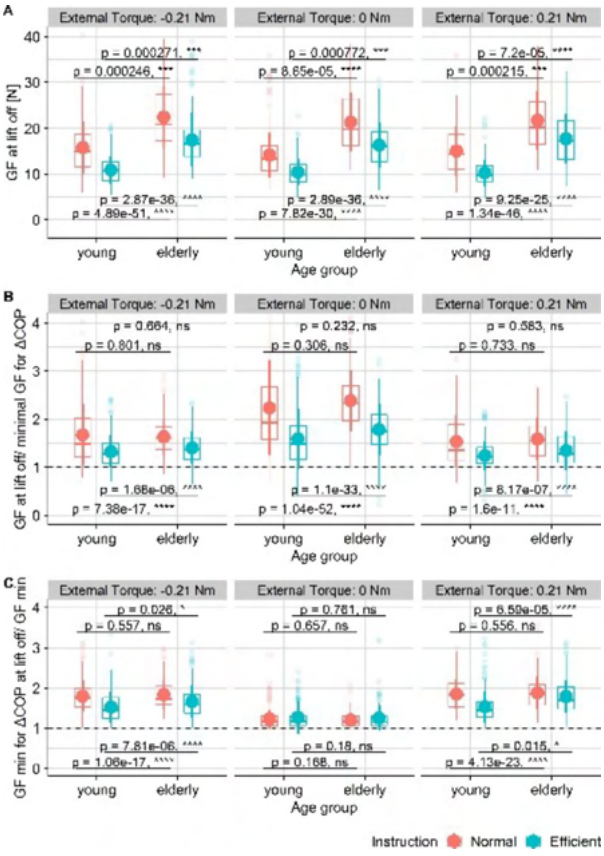

Figure 3: Mean GF and force rates GF/GF_(min at CoP) (~ safety ratio) and (GF_(min at CoP))/GF_min (~ force excess ratio due to deltaCoP deviations) at lift off for trials 3–6 per external torque.

Conclusion: Our findings demonstrate how task goals influence high-level motor control of object manipulation differentially in young and elderly participants and highlight the necessity to control for both instructions and friction when investigating GF control of neurologic patients.
Disclosure: We have no competing interests to disclose and received no targeted funding.

EPO-350

Prognosis of early and late MCI at the memory clinic in Thailand

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Background and aims: MCI is regarded as prodromal dementia. It is an unstable state. We aimed to observe the natural history of MCI registered at the memory clinic at Siriraj Hospital.
Methods: Individuals with mild cognitive impairment(MCI) from database at the memory clinic at Siriraj Hospital, Thailand (data being registered during 2008-2018) were included in this study. Neuropsychological(NP)-early mild cognitive impairment (EMCI) was defined as impaired memory and another cognitive domain. NP-late MCI(LMCI) was defined as deficits across all three cognitive domains.
Results: 388 with MCI were included. 84 were lost to follow up. Out of 304 with MCI that had follow up data with the mean follow up time of 36.5 months (SD 32 months), 53 were dead (17.43%), 95 cases were converted to dementia (31.25%). Only 96 had full neuropsychological evaluation at initial assessment and among these, 33 were EMCI and 63 were LMCI. There was no statistical difference in mean age, education and Thai mental state examination between EMCI and LMCI. Seven of early MCI (21.21%) and 29 of late MCI (46.03%) were converted to dementia (chi sq p=0.017*).

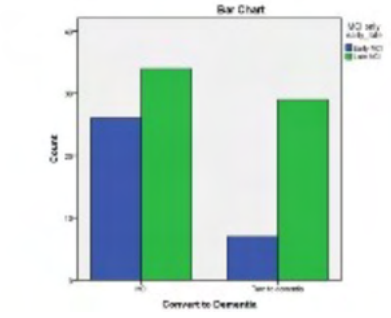

Figure 1. EMCI and LMCI conversion

Conclusion: MCI is not benign. NP-EMCI and LMCI had different prognosis in both dementia conversion and mortality.
Disclosure: Nothing to disclose.

EPO-351

The impact of arterial hypertension to blood-brain barrier permeability in patients with cerebral small vessel disease

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Background and aims: Cerebral small vessel disease (CSVD) is associated with arterial hypertension (AH). Thanks to novel neuroimaging techniques the effect of AH to brain damage could be found not only in white matter hyperintensities (WMH), but also in normal-appearing white matter (NAWM), but the causes of this interaction is not always clear. The aim is the assessment of the impact of AH to the blood-brain barrier (BBB) permeability in patients with CSVD.
Methods: The study included 46 patients (mean age 60.1±6.6, 30 women) with CSVD according to STRIVE criteria (2013) and the control group consisted of 10 volunteers (mean age 56.7±6.7 years, seven women). The BBB permeability was studied separately in WMH and NAMW using dynamic contrast-enhanced magnetic resonance imaging with volume transfer coefficient (Ktrans), fractional blood plasma volume (Vp) and the area under curve (AUC). All participants underwent 24-h ambulatory blood pressure monitoring (ABPM) for assessment mean and maximal values, standard deviation (SD) and the area under the curve (AUC) of daytime and nighttime systolic and diastolic blood pressure (SBP and DBP). The connections between parameters were studied with Pearson's correlation, where $p<0.05$ and $r>0.3$.
Results: Vp NAWN was connected with maximal daytime SBP (r=0.338) and DBP (r=0.308), daytime SBP-AUC (r=0.350). AUC NAMW was connected with maximal daytime SBP (r=0.317) and DBP (r=0.310), daytime SBP-AUC (r=0.465) and DBP-AUC (r=0.332), nighttime SBP-AUC (r=0.315).
Conclusion: The influence of AH on the development of CSVD is connected with the increased BBB permeability in NAWM.
Disclosure: Nothing to disclose.

EPO-352

Comparison of quality of life in women with episodic migraine, chronic migraine and focal epilepsy

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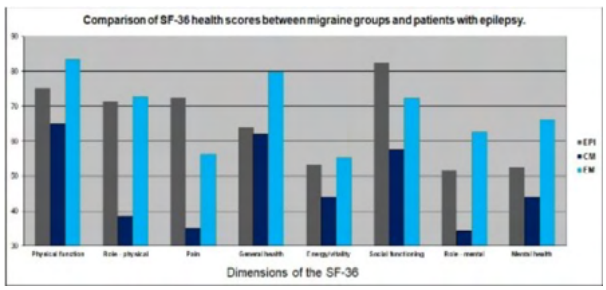
Background and aims: Migraine and epilepsy are frequent neurological conditions associated to a great social and individual burden
Methods: The purpose of this investigation was to compare self-reported health-related quality of life (HRQoL) in women suffering from partial epilepsy, episodic migraine and chronic migraine attending a tertiary care outpatient Unit (Hospital das Clínicas da USP-RP). Subjects were excluded if they had a history of any illness that might have confounded the association between epilepsy, migraine and quality of life. Sixty-two partial epilepsy, sixty-six episodic migraine and seventy chronic migraine consecutive patients entered the study and completed the validated Portuguese version of the generic instrument RAND 36- Item Heath Survey 1.0 – (SF-36). There is no significant difference among the groups concerning age and educational level. The eight SF-36 domains were compared across groups.
Results: Patients with chronic migraine reported significantly worse HRQoL compared to partial epilepsy on the role physical, pain, e social functioning. Significant differences between episodic and chronic migraine patients were found for seven domains, except vitality. Patients with partial epilepsy reported significantly worse HRQoL compared to episodic migraine on the general health and mental health.



Comparison of SF-36 health scores between migraine groups and patients with epilepsy

Conclusion: Several factors such as the social stigma associated to migraine and epilepsy, the Impact of epilepsy on employment status and the disabling accompanying symptoms of the migraine attacks could explain our results.
Disclosure: Nothing to disclose.

EPO-353

Alzheimer's Dementia and predictors of Driving Cessation: Results from a 4-year Longitudinal Study

P. Stamatelos [1], P. Chatzaki [1], I. Beratis [1], D. Pavlou [2], N. Andronas [1], S. Fragkiadaki [3], D. Kontaxopoulou [3], A. Mponakis [4], A. Economou [1], L. Stefanis [5], G. Yannis [2], S. Papageorgiou [1]
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Background and aims: Patients with Alzheimer's Disease Dementia (AD) face increasing driving difficulties as the disease progresses and, at some point, cease driving. We sought to identify predictors of driving cessation among patients with AD.
Methods: We examined 28 patients with mild AD (26 males, mean age 74 years old). Baseline evaluation included neurological and neuropsychological assessment and a driving simulator test. Re-evaluation after a mean period of 48 months included a structured interview with the patients and their caregivers. Primary endpoints were driving cessation and death.
Results: 10 patients died during follow up (35%, Mean time to death: 45 months), while 25/28 ceased driving (90%, Mean time to cease: 13 months). Main reason to cease driving was caregiver's concern (64%), followed by patients' will and Doctor's advice (18% and 14%, respectively). 60% of patients had at least one dangerous event during driving at follow-up period (accident, near-accident, disorientation). Performance (both time and errors) on Tandem Walking Test (modified with reverse number counting-mTWT) at baseline evaluation had a strong positive correlation with death probability ($r=+0.7$, $p=0.001$). Both IADL score and TMT-A time at baseline evaluation had a negative correlation with time to cease driving ($r=-0.6$, $p=0.034$). No statistically significant correlations were found between driving simulator measurements and primary endpoints, despite the tendency observed.
Conclusion: mTWT may be a promising marker of disease progression among AD patients. IADL and TMT-A may be used as predictors of driving cessation. Larger samples are possibly needed to establish correlations between driving simulator measurements and primary endpoints.
Disclosure: This study is part of Dr Stamatelos' PhD project with title " Evaluation of driving behavior of patients with MCI, Dementia or Parkinson's Disease: Diagnostic and Prognostic Markers", funded and supported by Onassis Foundation.

EPO-354

Yield of CSF dementia biomarkers in everyday clinical practice

P. Stamatelos [1], K. Kontokostas [2], C. Koros [3], V. Papastefanopoulou [4], E. Stanitsa [5], A. Bonakis [1], X. Arbaniti [1], K. Giannopoulou [1], L. Stefanis [6], J. Papatriantafyllou [7], C. Kroupis [1], S. Papageorgiou [1]
[1] Athens, Greece, [2] 1st University Department of Neurology, Athens, Greece, [3] Piraeus, Greece, [4] National and Kapodistrian University of Athens, Athens, Greece, [2] 1st University Department of Neurology, Athens, Greece, [5] 2nd Department of Neurology, Haidari, Greece, [6] Department of Neurology, Athens, Greece, [7] Department of Neurology, Athens, Greece

Background and aims: Cerebrospinal Fluid (CSF)-Alzheimer's Disease (AD) Biomarkers (total tau, p-tau and amyloid-beta 1-42) are recently available in Memory Clinics to facilitate the diagnosis of atypical dementia cases. However, their utility in everyday clinical practice is still under investigation.
Methods: Dementia cases, with at least one of the following atypical features: rapidly progressive course, early-onset, clinico-radiological discrepancy, were recruited from our Memory Clinic over a 3-year period (December 2016 – December 2019). Our sample consisted of 80 patients (Mean age 65.3 years, Women: 41). Clinical and radiological diagnosis was characterized as AD or non-AD by two dementia experts (SGP & JP) both unaware of the CSF findings. CSF Biomarkers were characterized as AD and non-AD based on the A/T/N (amyloid, tau, neurodegeneration) classification system-biomarkers' part. We then compared these different diagnostic approaches.
Results: In 60 patients clinical diagnosis was in agreement with radiological diagnosis (in 14 AD and in 46 non-AD). CSF Diagnosis was consistent to clinical and radiological diagnosis in 47 of these patients (in 9/14 AD and in 38/46 non-AD). In 20 patients the experts found a clinico-radiological discrepancy: 12 were AD clinically while non-AD radiologically and eight vice versa. CSF Biomarkers were indicative for AD in 6/12 and in 2/8, respectively. (See also Table 1)

Clinical	AD		non-AD		AD		non-AD	
Radiological	AD		non-AD		non-AD		AD	
CSF	AD	Non AD	AD	Non AD	AD	Non AD	AD	Non AD
N	9	5	8	38	6	6	2	6

Clinical, radiological and CSF Diagnosis in 80 dementia cases with atypical features (AD: Alzheimer's Disease, CSF: Cerebrospinal Fluid)

Conclusion: The above findings indicate that CSF AD biomarkers are helpful in everyday clinical practice for the accurate diagnosis in atypical dementia cases, especially in those with a clinico-radiological discrepancy.
Disclosure: Nothing to disclose.

EPO-355

Abstract withdrawn

EPO-356

Slovenian version of Alzheimer's Disease Assessment Scale–Cognitive Subscale (ADAS-Cog): standardisation and validation

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Background and aims: Alzheimer's disease (AD) is the most common type of dementia. The ADAS-Cog is a brief screening tool, which has been developed especially for detecting AD. The aim of our study was to standardise and validate ADAS-Cog for a cognitive screening of people with Mild Cognitive Impairment (MCI) and AD in the Slovenian population.
Methods: We included 46 people with cognitive impairment (26 MCI, 20 AD) and 45 healthy controls. All participants completed the Slovenian version of ADAS-Cog. Mean age, years of education, and ADAS-Cog score were compared between patients and healthy controls using unpaired t-test. Receiver operator curve (ROC) was drawn, and sensitivity, specificity, and likelihood ratio were calculated.
Results: People with cognitive impairment had significantly lower total ADAS-Cog score than controls (22.0 SD 10.3 vs. 8.0 SD 2.2 points, $p<0.001$). There were no statistically significant differences between groups in age or years of education. The area under the ROC for all patients was 0.97 (CI 0.93 to 1; $p<0.0001$). Optimal the cut-off for the ADAS-Cog was 11/12 points. Sensitivity was 94% (CI 82% to 98%), specificity 96% (CI 85% to 99%), and likelihood ratio 21.
Conclusion: ADAS-Cog is a reliable screening tool for cognitive impairment in people with cognitive impairment due to MCI or AD. The optimal cut-off score for Slovenian population is 11/12 points, which is similar to the other European countries.
Disclosure: Nothing to disclose.

EPO-357

The neuroinvasive phenotype of COVID-19's the community: data from Carnegie Mellon University's Delphi Group.

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Background and aims: There are accumulating clinical and translational studies that have confirmed and expanded the concept of SARS-CoV-2 neuroinvasive potential in the setting of COVID-19. The aim of our study was to determine COVID-19's neuroinvasive potential in the community using the survey results from Carnegie Mellon University's Delphi Group.
Methods: Data from December 2020's responders that had been tested for COVID-19 and received a positive / negative diagnosis (n=48,629; 12,117 COVID-19 positive) were used in this study. Among available symptom data, we defined COVID-19 associated potential neuroinvasion (COVID 18/PNI; PNI) as the simultaneous presence of headache, fever and nausea. Logistic regression was used to determine predictors of PNI among comorbidities, sex a nd age.
Results: COVID-19 / PNI was detected 1212 responders. A binary logistic regression model accounting for other symptoms, age, gender and comorbidities revealed that the major determinant of PNI was self-described immune system compromise, comprising the entirety of PNI (1,212/1,212). A multivariate logistic regression model adjusting for other symptoms, age and comorbidities revealed that PNI affected responders reporting all comorbidities except heart disease, sleep disturbances, sore throat, olfactory/gustatory symptoms, age between 65 – 74 years and non-binary gender / other gender (p-value<0.05). Out of these responders, only 30 (0.2%) were hospitalized.
Conclusion: Our study reveals a vulnerable population among in COVID-19 / PNI affects immunocompromised patients, known to have subtle or atypical symptoms even in bona fide meningitis / encephalitis. Given the low rate of hospitalization (0.2%) our findings mandate thorough clinical characterization of PNI.
Disclosure: Nothing to disclose.

EPO-358

Secondary Progressive MS treatment escalation identified algorithmically & clinically: A multi-registry based approach

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Background and aims: Disease modifying treatment (DMT) options for Multiple Sclerosis (MS) patients with a clinician diagnosed secondary progressive course (SPMS) are limited, leading to the common practice of off-label treatment with drugs approved for relapsing-remitting (RR) MS. Objective algorithms (OA) can identify SPMS in those with clinically assigned RRMS increasing the proportion of SPMS in MS registries, suggesting SPMS is under-diagnosed in clinical practice.
Objectives: To assess whether treatment intensity escalates as the disease evolves from RRMS to OA-SPMS and then to clinical SPMS where worsening is acknowledged with a change in diagnosis.
Methods: MS registries in the Czech Republic [Cz], Denmark [Den], Germany [Ger], Sweden [Swe] and the United Kingdom [UK] were used. Inclusion criteria were RRMS or SPMS; age 18 years. An OA was applied (Ramanujam et al. 2020). DMTs used at the date of the last recorded visit were classified as highly active (HA) or not, and in addition DMT use prior to the diagnosis of SPMS or OA-SPMS.
Results: Across the five registries 10808 SPMS patients were identified and 8385 OA-SPMS patients from the RRMS cohort. HADMT use was 21.3% (746/3495) prior to OA-SPMS diagnosis eg in RRMS (Den:19.4%;Cz:15.5%; Ger:19.6%;Swe:43.9%;UK:19.4%) and was 27.9% (1575/5644, OR 1.42, p<0.0001) once diagnosed (Den:34. 0%;Cz:23.3%;Ger:20.4%;Swe:63.7%;UK:26.2%). HADMT use was 23.5% (794/3375) prior to SPMS diagnosis (Den:20.2%;Cz:16.4%;Ger:27.2%;Swe:28.5%; UK:13.2%) and 36.9% (1381/3740, OR 1.9, p<0.0001) once diagnosed (Den:29.0%;Cz:22.7%;Ger:18.8%;Swe:75 .4%;UK:17.9%).

Conclusion: The evolution to clinical SPMS via OA-SPMS is resulting in treatment escalation by clinicians. However, this change is not, at least initially, driving a change in clinical classification.

Disclosure: The SPMS RCN Project is funded by Novartis. All research output is generated, analysed and written by the authors.

Cerebrovascular diseases 3

EPO-359

The impact of ACA occlusion on the short-term functional outcome of patients treated with mechanical thrombectomy

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Background and aims: Mechanical thrombectomy (MT) has been recognized as standard of care for anterior large vessel occlusions (LVOs) resulting in acute ischemic stroke (AIS). The aim of our study was to analyse the impact of anterior cerebral artery (ACA) occlusion on the short-term functional outcome of stroke patients treated with mechanical thrombectomy.

Methods: One hundred twenty-nine consecutive patients with LVO treated with MT were analyzed to identify all patients with associated ACA occlusion. Demographics, clinical, radiological and treatment characteristics were prospectively collected. Patients were divided into two groups by the presence of ACA occlusion on the first CT angiography. The functional outcome was mesured using modified Rankin scale (mRS) at 90 days, with mRS 2 defined as favourable functional outcome.

Results: ACA occlusion was detected in 15 (11.8%) patients. The smaller percentage of patients with ACA occlusion achieved favourable clinical outcome at 90 days (13.3% vs. 46.4%, p=0.023). Results of performed multivariate analysis showed that the higher initial National Institutes of Health Stroke Scale (NIHSS) score (OR 0.879, 95% CI 0.808–0.955, p=0.002), the presence of ACA occlusion (OR 0.155, 95% CI 0.025-0.941, p=0.043) and the appearance of complications during hospitalization (OR 0.099, 95% CI 0.036–0.274, p<0.001) were identified as negative predictors of favourable functional outcome.

Conclusion: The presence of ACA occlusion on the first angiography, together with the higher initial NIHSS score and the appearance of complications during hospitalization, predict less chances for a favourable functional outcome at 90 days.

Disclosure: Nothing to disclose.

EPO-360

Clinical characteristic of stroke mimics in patients underwent Code Stroke

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Background and aims: This study aimed to investigate the clinical and neurological characteristics of stroke mimics (SMs) among patients who underwent Code Stroke due to suspected acute stroke in the emergency room.

Methods: We conducted a retrospective review of all patients who underwent Code Stroke in an emergency room from January to December 2019. Baseline characteristics, laboratory findings, clinical and neurological features of SMs were compared with those of true strokes.

Results: A total of 409 patients underwent Code Stroke, and 125 (31%) patients were diagnosed with SMs. The common SMs were seizure (21.7%), drug toxicity (12.0%), metabolic disorders (11.2%), brain tumor (8.8%), and peripheral vertigo (7.2%). SMs were associated with female sex, younger than 50 years, history of epilepsy or psychiatric disorder, low NIHSS score, and low vascular risk factors. SMs were less likely to have typical stroke symptoms such as hemiparesis and dysarthria, while dizziness, mental change, and convulsions were more frequent. In neurological examination, hemiparesis (OR 2.80), upper limb monoplegia (OR 3.71), facial palsy (OR 7.9), gaze palsy (OR 3.47), visual field defect (OR 3.12), dysarthria (OR 1.99), neglect (OR 3.37) were more associated with stroke. Among the unilateral limb weakness, unilateral sensory changes, facial paralysis, dysarthria, aphasia, diplopia, and visual impairment, the likelihood of stroke increases as the number of accompanying focal neurological symptoms increases(p<0.001).

Conclusion: Some clinical and neurological characteristics have been shown to help differentiate SMs from a stroke. In particular, the accuracy of diagnosis can be improved through a combination of symptoms or neurological signs.

Disclosure: Nothing to disclose.

EPO-361

Acute aortic dissection presenting as painless, transient paraparesis

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Background and aims: Acute aortic dissection is one of the most dramatic cardiovascular emergencies. It usually manifests with thoracic and abdominal pain and hemodynamic instability; however, pain is absent in about 6% of cases.

Methods: A 77-years-old male presented with transient paraparesis that lasted approximately one hour two days before.

Results: He denied any neck, chest, or abdominal pain. His physical and neurological examination were unremarkable. His vital signs (including blood pressure in both arms) were normal, and pulses were strong and symmetric in both upper and lower limbs. The transthoracic echocardiogram findings were compatible with ascending aorta dissection and further computed tomography angiography workup revealed a type-A aortic dissection, which extended from the aortic orifice to the origin of the superior mesenteric artery. Magnetic resonance imaging of cervical and thoracic spinal cord was normal. The patient was treated with medical blood pressure control without surgical intervention and had a good clinical outcome.

Conclusion: Neurological complications of aortic dissection are rare and most commonly include ischemic stroke, ischemic neuropathy, and spinal cord ischemia. The latter results from occlusion of the origin of various arteries, mainly the artery of Adamkiewicz. Transient neurologic symptoms are generally attributed to temporary occlusion of the vessel origin by movement of intimal flaps or decompression of the false back into the true lumen. Our case illustrates that painless, transient neurologic deficit can be the only presenting symptom of acute aortic dissection and that it should be part of the differential diagnosis of acute paraparesis.

Disclosure: Nothing to disclose.

EPO-362

Epidemiology of CVT in Slovenia: impact of COVID19 pandemic

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Background and aims: Background and aims: Cerebral venous thrombosis (CVT) is a rare cause of stroke with a highly variable clinical presentation and prognosis. To prevent further brain damage, prompt diagnosis and initiation of anticoagulant therapy are crucial. During COVID19 pandemic our healthcare resources have been severely challenged. Our objective was to determine the clinical, epidemiological and radiological characteristics of CVT in the Savinja Statistical region (part of Slovenia).

Methods: A retrospective analysis of records of all the patients with CVT admitted to General Hospital Celje from 01.01.2013 to 31.12.2020.

Results: There were 20 patients with CVT. The median value of age of CVT patients was 48 (average 47.25), with a female/male ratio of 1.5. Median value of initial NIHSS score was 1.5 and decreased to 0 at discharge. The mortality rate was low – 5%. Clinical presentation was very diverse; focal neurological signs (including seizures) were the most common finding and occured in 40% of all cases. Headache was the most frequent symptom of CVST and occured in 55% of all cases. Ischemic stroke with hemorrhagic transformation was present in 35% of patients with CVT. The most frequent risk factors were genetic and acquired prothrombotic conditions, None of the patients had a history or concurrent COVID19 infection.

Conclusion: No direct association with COVID19 infection was found, however the increase in CVT incidence due to other infective causes such as mastoiditis suggests a possible deleterious association of CVT incidence due to decreased availability of healthcare resources during the pandemics.

Disclosure: Nothing to disclose.

EPO-363

Factors associated with internal carotid artery tortuosity in patients with sporadic cerebral small vessel disease

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Background and aims: Cerebral small vessel disease (SVD) accounts for approximately 20% of all strokes and up to half of all dementias. Also is known, that internal carotid artery (ICA) tortuosity is associated with MRI-defined markers of SVD. This study aimed to reveal the factors associated with ICA tortuosity.
Methods: 53 consecutive non-diabetic patients (16 (30.2 %) men, mean±SD (Me) of age – 59.1±9.0 (59.0) years) with sporadic SVD were retrospectively analyzed. Carotid arteries were imaged bilaterally with a standardized protocol. ICA tortuosity presence, common carotid intima-media thickness, maximum blood flow velocity of superior ophthalmic vein (SOV) and vein of Rosenthal were assessed. Systolic blood pressure (BP), diastolic BP, lipid profile (total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglycerides), fasting plasma glucose, fibrinogen, total white blood cell count, absolute neutrophil count, erythrocyte sedimentation rate (ESR) were determined. Logistic regression was used to evaluate factors associated with ICA tortuosity.
Results: 21 (40.4 %) patients had ICA tortuosity. Univariate analysis showed that the presence of ICA tortuosity was positively associated with the maximum blood flow velocity of SOV (OR 8.5, 95% CI 1.4–53.8, p=0.023), ESR (OR 3.1, 95% CI 1.2–8.1, p=0.018) and age (OR 1.1, 95% CI 1.0–1.2, p=0.016) among the other factors determined including patient sex. On the other hand, only age was significantly associated with the presence of ICA tortuosity by multivariate logistic regression (B=0.122, OR=1.1, 95% CI 1.0–1.2, p=0.013).
Conclusion: Maximum blood flow velocity of SOV, ESR and age are associated with ICA tortuosity presence and, accordingly, with sporadic SVD.
Disclosure: Nothing to disclose.

EPO-364

MicroRNA-126 role in atherosclerosis and cerebrovascular disease.

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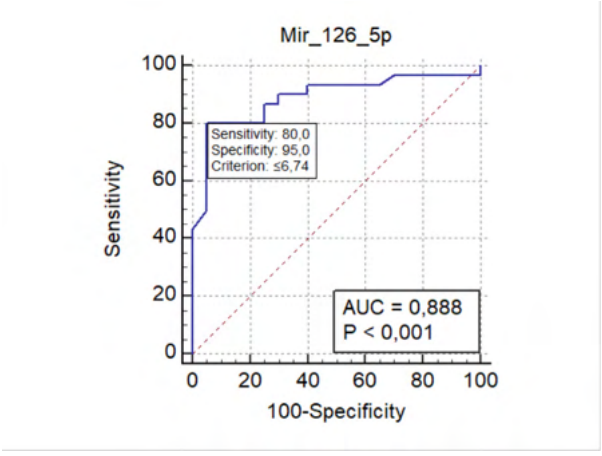
Background and aims: Atherosclerosis (AS) and its complications are main cause of disability and death worldwide, strongly associated with cerebrovascular disease (CVD). Noncoding RNAs - microRNAs (miRs) are involved in biological pathways of AS. MiR-126 negatively regulates vascular cell adhesion molecule 1 (VCAM-1) and it's atheroprotective role of miR-126 family was enlighten, so in this study we aimed to identify its expression level.
Methods: 61 people with CVD enrolled in this study. All patients were divided into two groups: internal carotid artery (ICA): 50% (group I) and less than 50% (group II) identified by ultrasound (according to European Carotid Surgery Trial (ECST) criteria). Mean age – 66 [61;71] years. Clinical (neurological status, cognitive tests) and laboratory (coagulogram, biochemical and blood routine data) tests were carried out. MiR extraction and quantification were performed with special validated kits and primers.
Results: The most common comorbidities were hypertension and diabetes mellitus. Cognitive impairments were more severe in patients of 1st group (21,5±2,8 versus 24+2,3 according MoCA test). The levels of MiRs were statistically different between groups (×ten to the sixth power copies): miR-126-5p (5.7 versus 9.4 p<0,001), miR-126-3p (6.64 versus 8.7 p<0,001). The model checked by ROC analysis the area under the curve (AUC) was 0.89 for miR-126-5p. Routine blood tests didn't show relevant differences.
Conclusion: MiRs can be promising biomarkers of advanced AS. Studied MiR were downregulated and this proves that MicroRNA-126 family play ateroprotective role.



ROC-analysis of selected miRNA

Disclosure: The authors declare no conflict of interest.

EPO-365

Natural Killer Cells functional activity disorders in acute period of Experimental Hemorrhagic Stroke

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Background and aims: The study of risk factors for the development of infectious and inflammatory complications and ways to reduce them in hemorrhagic stroke is a topical neurological problem. Assessment of the functional activity of Natural Killers ells in the acute period of experimental hemorrhagic stroke (EHS) of varying severity grades was the aim of this study.
Methods: In this experimental study the functional activity of spleen NK-cells was studied on five groups Wistar Rats (control, sham-operated, mild EHS, moderate EHS, severe EHS; weigh: 200–220 g., n=50) with varying severity grades of EHS. EHS was carried out by stereotaxic cutting the vessels in capsula interna of left hemisphere (ML=2.6 mm; AP=1,5 mm; DV=6 mm). The functional activity of spleen NK-cells was assessed using flow cytometry.
Results: It was shown that in animals on the 7th day of EHS there was a decrease in the functional activity of spleen NK-cells with significant differences – EHS with mild grade: 20 (19; 23)%, =0.00124, EHS with moderate grade: 19 (17; 21)%, =0.00004, EHS with severe grade: 18 (16; 22) %, =0.00004. Disorders of the functional activity of NK-cells are more expressed in the EHS model of moderate and severe grade of severity.
Conclusion: It has been shown that EHS leads to development of decrease in the functional activity of spleen NK-cells. With increasing grade severity of EHS, the functional activity of NK-cells is impairing.
Disclosure: The study had no sponsorship.

EPO-366

Prognostic value of neuron-specific enolase for assessment of the functional outcome in acute ischemic stroke patients

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Background and aims: The management of patients with ischemic stroke (IS) is largely based on the prognosis of the outcome. Identifying predictive biochemical markers can improve the accuracy of this prognosis. One of these neuro-biochemical proteins can be Neuron-specific enolase (NSE), which is known as a marker of neuronal damage. The aim of the study was to estimate the prognostic value of NSE in acute IS patients.
Methods: 50 patients (mean age 66.5±10.4 years) with 1st-ever acute IS were examined by the National Institutes of Health Stroke scale (NIHSS), modified Rankin scale and the Rivermid Mobility Index performed on admission to the hospital and 12–14 days after stroke. The plasma NSE level was measured at 1st 48 hours of IS onset. NSE was analyzed by commercially available ELISA kit.
Results: NSE significantly (r=0.33, p=0.02) correlated with NIHSS score at the time of admission and volume of the ischemic focus (r=0.49, p=0.003). NSE lever less than 2ng/ml was associated with favorable functional outcome as well as a significant recovery of motor function 12–14 days after the IS onset (OR=12.4, p=0.006 and OR=5.8, p=0.02 respectively).
Conclusion: Plasma concentrations of NSE have a high predictive value for favorable functional outcome and significant recovery of motor function after acute IS.
Disclosure: Nothing to disclose.

EPO-367

Ripped-off speech: an uncommon cause of carotid artery dissection.

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Background and aims: In young adults, ischemic stroke is rare (10–15% of all strokes). Etiology ranges from genetic conditions, hematologic or inflammatory diseases, and connective tissue disorders. Among these, carotid artery dissection (CAD) is most common.
Methods: Case report.
Results: A 38-year-old male motorbiker with no comorbidities presented to ED with global aphasia and right-sided hemi- and facial paresis (NIHSS 16). On CT, a demarcated frontal lobe infarction was present. CTA demonstrated long left internal carotid artery (ICA) occlusion resulting in arterio-arterial embolism to the left anterior M2 middle cerebral artery (MCA). He was admitted to the stroke unit, treated as per protocol. Additional information revealed that the patient had reported left-sided facial and neck pain within the previous week. There was no history of trauma. On re-examination, mild left-sided ptosis and miosis were noted. MRI confirmed the clinical suspicion of internal CAD. Prominent styloid processes (right: 45mm, left: 50mm) were found in direct contact with left ICA and in proximity to right ICA (2mm). No other causative factors for CAD were discovered. EPO112 Neurorehabilitation was started and subsequent surgical correction of styloid processes was planned.
Conclusion: Eagle syndrome (ESy) is defined by a calcified stylohyoid ligament or an elongated styloid process, impinging on surrounding structures, which may result in CAD due to direct mechanical insult. In contrast with idiopathic CAD, where the dissection frequently improves without invasive intervention, surgical treatment is required to prevent recurrences. In patients with CAD, ESy recognition is crucial to ensure optimal patient management and improve long-term prognosis.
Disclosure: Nothing to disclose.

EPO-368

Glycemic Gap Predicts Outcome of Patients with Intracerebral Hemorrhage

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Background and aims: The relationship between admission hyperglycemia and intracerebral hemorrhage (ICH) outcome is still controversial. Glycemic gap (GG) can reflect glucose homeostatic response to physical stress better than admission glucose levels. We aimed to evaluate the association between GG and in-hospital mortality in ICH.
Methods: We retrospectively identified consecutive patients hospitalized for spontaneous ICH at the two healthcare systems in the Twin Cities area, MN. Demographics, medical history, admission laboratory and computed tomography data were recorded. GG was estimated using admission glucose level minus HbA1c-derived average glucose. The association between GG and in-hospital mortality was evaluated by Cox regression analysis. Receiver operating characteristic (ROC) analysis was used to evaluate the ability of GG to predict in-hospital death.
Results: Among 345 included patients, 63 (25.7%) died during the hospital stay. Compared with survivors, non-survivors presented with a higher National Institutes of Health Stroke Scale score, larger hematoma volume, and higher glucose and GG levels at admission ($p<0.001$). At Cox regression analysis, GG resulted an independent predictor of in-hospital mortality after adjusting for potential confounders ($p<0.05$). GG showed a good discriminative power (area under the ROC curve: 0.75) in predicting in-hospital death and performed better than admission glucose levels in diabetic patients.
Conclusion: The GG is associated with the risk of in-hospital mortality and can represent a simple tool to assess the prognosis of diabetic patients with acute ICH.
Disclosure: Nothing to disclose.

EPO-369

Cytokines and growth factors in primary vasculitis of internal carotid and vertebral arteries

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Background and aims: Primary vasculitis (PV) of the internal carotid artery (ICA) and vertebral artery (VA) is a little-known cause of ischemic stroke (IS) with poorly understood pathogenetic mechanisms.
Methods: We studied 25 patients (17 men, 68%, mean age – 36.2±5.7 years) with ICA/VA PV verified by high-resolution vessel-wall MRI (by arterial-wall thickening and contrast enhancement). Systemic vasculitis, atherosclerosis and dissection were excluded. Interleukin (IL) 1, IL-2, IL-6, IL-17, tumor necrosis factor alpha (TNF), transforming growth factor beta 1 (TGF-1) and basic fibroblast growth factor (bFGF) were analyzed by enzyme linked immunosorbent assay (ELISA). The control group consisted of 21 healthy volunteers (14 men, 67%; mean age - 35.3±10.2 years).
Results: The levels of following cytokines and growth factors were increased in patients with ICA/VA PV compared to the control: IL-2 (5.64±1.82 pg/ml vs 4.30±1.65pg/ml, p=0.013), IL-6 (8.19±3.89 vs 4.7±1.48 pg/ml, p=0.000), TNF-a (36.9±33.66 vs 12.68±5.93 pg/ml, p=0.000), TGF-1 (2.77±1.60 vs 1.63±0.64 pg/ml, p=0.006) and bFGF (417.67±132.68 vs 335.71±105.08 pg/ml, p=0.018). The levels of IL-1 and IL-17 did not differ significantly from the control.
Conclusion: Proinflammatory cytokines produced by Th17 and Th1 CD4+ lymphocytes as well as FGF and TGF-1 play a role in the pathogenesis. Normal levels of IL-1 and IL-17 suggest that they are not significant in the development of local inflammation in ICA/VA PV, in contrast to systemic vasculitis such as giant cell arteritis. Understanding the pathogenesis of ICA/VA PV is essential for choosing the most optimal tactic and developing new approaches to treatment that pathology.
Disclosure: Nothing to disclose.

EPO-370

Data Safety And The Effectiveness Of The Electronic Stroke Registry Work In Kyrgyzstan: From Bishkek To Remote Regions

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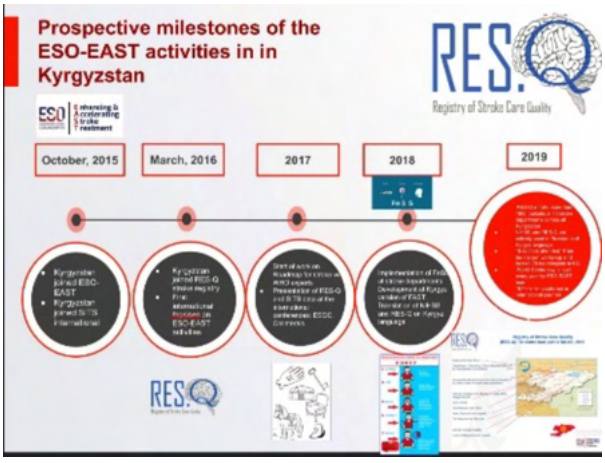
Background and aims: Electronic stroke registry RES-Q is an unique registry initiated by ESO EAST Committee. Logistics, risk factors, therapeutic approaches and outcomes in stroke patients are analyzed, keeping all the GDPR standards and supporting research in more than 50 countries. We aimed to describe the advantages in the conducting of research in the RES-Q stroke registry in Kyrgyzstan in the framework if the E-Health development.
Methods: 24 variables were analyzed in 2126 stroke patients admitted to 12 stroke departments in the period 2016–2020 in Kyrgyzstan.
Results: Patients data received by the local and national coordinator in a unified file with demographic and clinical variables, are individually coded, encrypted and GDPR-protected. Stroke is prevalent in males (53%) with 64% of ischemic type. Males with stroke in Kyrgyzstan are significantly younger with a median age of 61 vs. 67 in females, p=0,0001, due to low hypotensive and statin therapy adherence (32%), smoking and repeated strokes without prevention measures. Ischemic stroke prevails all over Kyrgyzstan, but the rate of intracerebral hemorrhage is higher in rural areas and highland aborigens tend to deny hypotensive treatment.



RES-Q stroke registry milestones in Kyrgyzstan

Conclusion: For five years RES-Q registry effectively has been and safety led in Kyrgyzstan, detecting the main problems of stroke logistics: low stroke awareness and medication adherence in population, and absence of advanced imaging in state hospitals. RES-Q allowed stroke situation clinical and epidemiological assessment with attempting of its implementation on the governmental level.
Disclosure: Nothing to disclose.

EPO-371

Implantable Loop Recorder to detect Atrial Fibrillation in Cryptogenic Stroke: a real-world experience

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Background and aims: Paroxysmal atrial fibrillation (AF) represents one of the main mechanisms underlying cryptogenic stroke (CS). Trials have shown that prolonged cardiac monitoring through Implantable Loop Recorders (ILR) allows higher AF detection frequency after CS compared with routine follow-up and 24-hour Holter monitoring, reaching 30% rate at three years. We aimed at assessing whether these data are reproducible in clinical practice.
Methods: From July 03, 2018 to December 30, 2020, 81 CS patients were implanted with ILR after that extensive testing (24-hour ECG monitoring, echocardiography, head and neck computed tomography angiography) had not revealed a definite etiology. Exclusion criteria were anticoagulant therapy contraindication, scarce compliance, and short-term poor prognosis. ILR online transmissions were regularly checked by neurologists; arrhythmias alarms were reviewed by cardiologists.
Results: Out of 109 hospitalized CS patients, 81 (74.3%) (mean age 72.3 years, range 49–88) were subjected to ILR. Median follow-up time from implantation is currently 381 days (range 4–915). AF was detected in 23/81 (28.8%) patients after a median time of 102 days (range 13–520). Three patients had ischemic stroke recurrence. In one case, AF was not detected; one had ischemic stroke recurrence after five months from AF diagnosis and anticoagulation start due to internal carotid artery plaque; the last was waiting for anticoagulants starting after AF diagnosis.
Conclusion: ILR is feasible and effective to detect occult AF after CS, with higher sensitivity compared to short-term monitoring. Our results suggest that up to 30% of CS patients may have AF as underlying stroke etiology.
Disclosure: Nothing to disclose.

EPO-372

Don't forget melas syndrome

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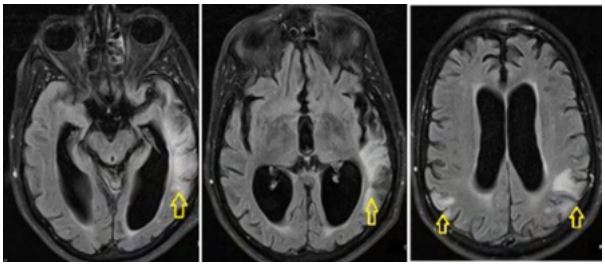
Background and aims: MELAS syndrome (Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes) is an infrequent disorder, but one of the most frequent maternally inherited mitochondrial disorders.
The most common mutation associated with MELAS syndrome is the m.3243A>G mutation in the MT-TL1 gene encoding the mitochondrial tRNA.
Methods: A 36-year-old man was followed up for six years for an episode of language disturbance (he presented phonetic and semantic paraphasia) and for several episodes of generalized tonic-clonic seizures. In the initial MRI he presented subacute ischemic lesions in the left occipital and left temporal bones, chronic ischemic lesions in both cerebellar hemispheres and multiple chronic cortico-subcortical ischemic lesions of diffuse location. After studying negative thrombophilias and other autoimmune diseases, he was diagnosed with MELAS Syndrome.
Results: The patient is currently being treated with L-Arginine, a precursor of nitric oxide that favors cerebral vasodilation and has a positive effect on the aerobic metabolism of the muscle (used in acute flare-ups and as maintenance therapy), as well as Coenzyme maintenance. Q10 and Rivoflabine, intermediate metabolites of the mitochondrial respiration chain, and creatine, one of the substances that is decreased in these mitochondrial myopathies without knowing the reason. Also, in antiepileptic treatment with perampanel and levetiracetam.



Cerebral magnetic resonance

Conclusion: It is an infrequent pathology, but it must be considered, because although there is no etiological treatment, a relatively effective symptomatic treatment can be carried out compared to what is used in the case of stroke of ischemic origin.
Disclosure: Nothing to disclose.

EPO-373

Prolonged ECG Monitoring for 21 days in ESUS. Is it enough time?

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Background and aims: Long-term electrocardiogram (ECG) monitoring for 30 days has showed to be effective for atrial fibrillation(AF) detection in Embolic Strokes of Undetermined Source (ESUS). We analyze its diagnostic yield in a shorter period of 21 days.

Methods: Prospective, observational study on ESUS patients under going 21-days monitoring . Subjects with >3 Modified Rankin score and/or poor family support were excluded. Wearable Holter device (Nuubo™) as well as Nuubo Leonardo reading software were used. 23 hours per day were recorded and it took 1 hour to recharge the battery. The recording analysis was performed by a cerebrovascular disease specialized neurologist after three weeks. AF was interpreted on those irregular R-R interval alerts with a >30 seconds duration.

Results: 104 patients were enrolled, 54 females and 50 males, with 67 year-old median age. The median NIHSS at the admission was 3. 32 patients (30,8%) revealed silent chronic isquemic lesions in MRI, and 19 subjects had previuosly suffered a stroke. The median valid recording percentage was 90,5%. 22 patients (21,5%) were diagnosed with AF, which appeared during the first two weeks in the 75% of the cases. The Number Needed to Screen AF (NNS) was 5.

Conclusion: The diagnostic yield of 21-days ECG monitoring could be comparable to 30-days classical long-term studies, allowing for optimization of time and resources

Disclosure: Nothing to disclose.

Cognitive neurology/neuropsychology 2

EPO-374

Differences in spontaneous eye blink rate as a function of clinical diagnosis in prolonged Disorders of Consciousness

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Background and aims: Diagnosis of Disorders of Consciousness (DoC) is based on clinical interpretation of patients' behavioral responses to multisensory stimulation, that could be hindered by cognitive and sensory-motor impairments. In order to improve accuracy and speed of the diagnostic process, we investigated whether spontaneous eye blink rate (EBR), a reliable behavioral correlate of cognitive activity in healthy individuals, could be used as a covert proxy of patients' level of responsiveness.
Methods: In a within-subject design, patients' eye blinks were collected by online visual identification during two auditory oddball tasks, i.e. passive listening to tones and active counting of target tones, and the preceding and concluding 3-min rest phases. After the experimental sessions, a further offline electro-oculographic check was performed confirming patients' EBR.
Results: Six patients in Vegetative State/Unresponsive Wakefulness Syndrome (VS/UWS; one female; mean age=50.2±14.3 years; mean time post-injury=2.5±1.5 months) and nine patients in Minimally Conscious State (MCS; two females; mean age=56.2±10.6 years; mean time post-injury=3.4±4.6 months) were enrolled in post-acute phase. Patients' EBR was stable within and across sessions, with no differences across experimental conditions for VS/UWS or MCS, respectively. However, patients in MCS exhibited a significantly higher EBR than patients in VS/UWS; moreover, EBR positively correlated with the Coma Recovery Scale-Revised Index.
Conclusion: Our results suggest that monitoring patients' EBR, a measure easy to collect in clinical practice, for few minutes at rest could contribute to reduced rates of misdiagnosis in patients with DoC.
Disclosure: The authors report no disclosure.

EPO-375

Cognitive disorders as markers of anxiety and depression in patients with kinking of the internal carotid arteries

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Background and aims: Currently, the management and treatment of patients with kinking of the internal carotid arteries (ICA) are contradictory. Complaints of patients with ICA kinkings are non-specific and differ in clinical diversity. The aim of the study was to analyze the frequency, structure and relationship of psychoemotional and cognitive disorders in patients with ICA kinkings.
Methods: The prospective study included 127 patients with hemodynamically significant ICA kinkings (main group) in age from 24 to 66 years and 48 responders the same age without kinkings (control group). Hospital Anxiety and Depression Scale (HADS) was used to evaluate anxiety and depression, considering them if the score was10. To detect cognitive dysfunction, all patients underwent the Montreal Cognitive Assessment scale (MoCA) – normal values are 26–30 points). The data were analyzed with IBM SPSS Statistics and MS Excel software.
Results: The mean age of patients was 56.5±16.4 and 58.2±17.1years in both groups respectively. According to the HADS, anxiety was detected in 33.8% and 31.2% patients, depression in 11.8% and 10.4% of patients in main and control groups respectively. According to the MoCA scale, cognitive impairment was detected in 30.7% and 29.8% of respondents of both groups respectively. In patients with ICA kinkings with reduced cognitive functions, the levels of anxiety (12.3±1.8 and 5.7±1.6, $p<0.05$) and depression(11.2±1.6 and 3.5±1.2, $p<0.05$) was significantly higher.
Conclusion: In patients with kinkings of ICA cognitive disorders most likely due to anxiety and depression but not to morphological changes of artery.
Disclosure: Nothing to disclose.

EPO-376

Functional and structural MRI correlates of executive function impairment in multiple sclerosis

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Background and aims: To investigate resting state (RS) functional connectivity (FC) and white matter (WM) microstructural abnormalities underlying executive function (EF) impairment in multiple sclerosis (MS) patients.
Methods: One-hundred and sixteen MS patients and 65 age- and sex-matched healthy controls (HC) underwent brain 3T MRI, including T1-weighted, RS and diffusion-weighted sequences; and neuropsychological evaluation with a computerized version of Wisconsin Card Sorting Test (WCST). The main large-scale brain cognitive functional networks were derived with independent component analysis. Mean fractional anisotropy (FA) was calculated for a priori-selected WM tracts. Abnormalities in RS FC and FA were investigated. Associations of MRI abnormalities with standardized WCST scores were investigated with age- and sex-adjusted step-wise multivariable linear models.
Results: In MS-patients, independent predictors of worse working memory/updating (WCST achieved categories) were: lower corpus callosum (CC) genu FA, working-memory network (WMN) left precuneus, right superior and middle temporal gyri RS FC; higher default-mode network (DMN) right superior occipital gyrus, salience network (SN) right superior frontal gyrus (SFG) RS FC (R2=0.35). Independent predictors of worse attention (WCST errors) were: lower CC genu FA, WMN left precuneus, DMN right anterior cingulate gyrus RS FC; higher WMN right cerebellum lobule 9, ECN right SFG RS FC (R2=0.24). Independent predictors of worse inhibition (WCST perseverative errors/responses) were: lower CC genu and right superior cerebellar peduncle (SCP) FA, WMN left precuneus RS FC; higher ECN right SFG RS FC (R2=0.24).
Conclusion: CC genu and right SCP microstructural damage, and RS FC abnormalities in cognitive networks underlie EF frailty in MS.
Disclosure: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

EPO-377

Effect of vitamin D supplementation on cognitive function at six months after a stroke: a randomized clinical trial

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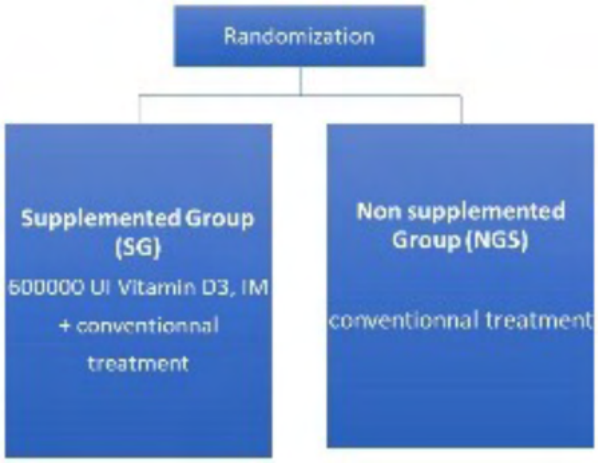
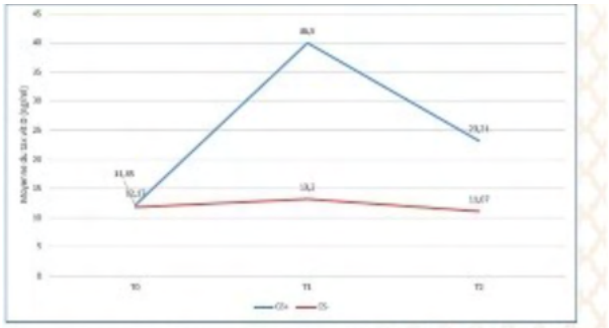
Background and aims: Vascular cognitive impairment occurs in 10% to 82% of patients at six months after a stroke. Vitamin D deficiency is very common in this population and may be a factor influencing the cognitive prognosis. The aim of this study is to determine the effect of vitamin D supplementation on overall cognitive function at six months of a 1st ischemic or hemorrhagic stroke.
Methods: This is an interventional study type. We included patients with a 1st ischemic or hemorrhagic stroke and suffering from vitamin D deficiency. The sample was randomized into two groups. One group received vitamin supplementation (600,000 IU vitamin D3 IM) with the conventional treatment protocol and the other group received the conventional treatment protocol only. The assessment of overall cognitive function took place at six months using The Montreal Cognitive assessment (MoCA).



Results: We included 147 patients. About 62% of participants presented a global cognitive impairment at six months. Vitamin supplementation did not result in an improvement in cognitive function at six months. The proportion of patients with cognitive impairment was comparable between the two groups (62.2% vs. 61.8%, p= 0.96). We studied its effect according to age, gender, type of stroke, stroke severity and initial vitamin D status. Supplementation had a statistically significant benefit and reduced the occurrence of cognitive impairment for male patients (64.7% vs 35.7%, OR = 3.3 (95% CI, [1.16-9.38], p=0.02)).



The change in vitamin D levels on assessment at 3 and 6 Months

Conclusion: Vitamin D supplementation may have provided some protection for certain subgroups. Optimization of the supplementation protocol may offer more encouraging results.
Disclosure: Nothing to disclose.

EPO-378

Chess and brain performance

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Background and aims: Chess is an intellectually complex game, strategically demanding and highly competitive, which requires the orchestration of various psychological functions, including attention, perception and memory. This review aims to provide an overview of the findings regarding the influence of chess on the brain.
Methods: Bibliographic research was carried out in reliable databases (PubMed, Scielo and Web Of Science) between the years 1990 to 2020, the descriptors used were "chess" and "brain" combined with Boolean operators. The most relevant articles were considered for the review of narrative literature.
Results: It was shown that masters and great masters of chess showed increased activation in neural networks involved in the control of cognitive functions, such as attention, executive functions and problem solving, parts mediated by the thalamus. In a comparison between masters and novices, it was demonstrated that experienced players achieved a reduction in the volume of gray matter bilaterally in the caudate nucleus. The caudate nuclei of great masters and masters were significantly smaller compared to those of beginners, but exhibited a reinforced connection with the network in a standard way in spontaneous oscillatory activity, which led to the hypothesis of synaptic "pruning", where redundant synapses are eliminated from the brain, accelerating and increasing the efficiency of the response to stimuli.
Conclusion: Studies have concluded that the gray and white masses are altered when comparing experienced players to controls, however, further studies should be performed to elucidate the anatomical differences.
Disclosure: We don't have any conflicts of interest.

EPO-379

Comparison of decision making in patients with temporal and frontal lobe epilepsy

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Background and aims: Although the effect of the frontal lobe on cognitive functions is a subject that has been studied frequently, cognitive impairments that can be seen in frontal lobe epilepsy are less frequently addressed. Two of the main neural networks required for decision making are located in the prefrontal cortex and amygdala. In this study, we aimed to compare the decision making performance of cryptogenic FLE and TLE patients in ambiguous situations.
Methods: Twenty TLE patients (mean age;34,10±11,71, eight male) and 20 FLE patients (mean age;32,25±11,92, 10 male) were enrolled in the study and their cognitive performance was compared with 20 healthy controls (mean age;33,15±13,66, 11 male) without neurological and psychiatric diseases matched with age, sex and years of education. Neuropsychological tests were applied to the participants for sleep, depression, anxiety, impulsivity, intelligence, attention, language functions, memory and learning, frontal axis functions. Decision making performance in ambiguous situations was studied with the Iowa Gambling task.
Results: IGT performances of FLE and TLE patients were found to be worse than healthy controls (p=0,049). Although there was no statistically significant difference when the decision making of TLE and FLE patients was compared, it was observed that FLE patients chose higher risk cards compared to TLE patients. Performance of the neuropsychological subgroup tests of TLE and FLE patients in attention, language functions, memory and learning, frontal axis functions were found to be significantly worse than healthy subjects.
Conclusion: TLE and FLE patients' decision making in uncertain situations is similarly impaired compared to healthy controls.
Disclosure: There is no conflict of interest.

EPO-380

Effectiveness of biofeedback training based on the brain-computer interface in poststroke patients.

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Background and aims: Post-stroke cognitive impairment (PSCI) is an important problem in the rehabilitation of patients after stroke. They reduce treatment compliance and inhibit patient resocialization. In the rehabilitation of such patients, one of the most promising methods is using of biofeedback cognitive training based on a brain-computer interface (BCI). The purpose of this study is to evaluate the effectiveness of cognitive training in patients with PSCI.
Methods: The study included 15 patients. Cognitive impairment was assessed using Montreal Cognitive Assessment (MOCA). To assess affective disorders, we used the Hospital Anxiety and Depression Scale (HADS). Testing was carried out before and after a course of cognitive training (8-10 sessions). Trainings were conducted on neuro-headset «GARANT-EEG» (NeuroChat, Russian Federation) which performs the function of BCI, allows the patient to mentally control the flow of visual and verbal information on the monitor screen.

The patient performs cognitive training tasks using the brain-computer interface.

Results: Positive results were obtained during the study. The score on the MoCA before the onset of training averaged 21.67±2.16 points, after - 24.27±1.94 points, the results are statistically significant ($p < 0.001$). According to the HADS, the average level of anxiety before the course was 4.46±1.68 points, after – 3.20±1.14 points; the average level of depression before the course was 4.5 ±2.23, after – 3.66±1.83 ($p < 0.005$ for anxiety, $p < 0.01$ for depression).
Conclusion: The study showed that biofeedback training based on the BCI is promising for further study as a method of neurorehabilitation for patients with post-stroke cognitive impairment.
Disclosure: There is no conflict of interest.

EPO-381

A Multinational Qualitative Study Examining the Intergenerational Burden of Huntington's Disease (part of SEEING-HD)

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Background and aims: Huntington's Disease (HD) is a complex hereditary and progressive neurological disease characterised by cognitive, behavioural and motor symptoms. The overall burden of HD across generations of families remains under-studied and thereby limits our ability to make evidence-based decisions about the care and support needed for those affected by HD. SEEING-HD aims to explore the intergenerational burden of HD.
Methods: Building on a systematic literature review conducted in the 1st phase of SEEING-HD, a qualitative research study is being designed to address current evidence gaps related to the quality of life and socioeconomic burden associated with HD. The study will include ~60 qualitative semi-structured video/telephone interviews with individuals with HD (across disease stages), their families (who may also have HD) and healthcare practitioners (e.g. clinicians, nurses) across seven European countries. A content analysis approach will be used to analyse transcripts of audio/video recordings using Atlas-ti software for coding and retrieval of qualitative data. Common themes and concepts attributable to various participant subgroups will be highlighted in a conceptual model of the intergenerational burden of HD.
Results: A study protocol detailing the target population and subgroups (e.g. by disease stage, generation, country), quantitative and qualitative data collection and analytic approach will be presented at the conference.
Conclusion: By examining the burden of HD from a multidimensional, generational perspective, findings from this study will significantly contribute to the knowledge base and empower healthcare professionals and policymakers to advance evidence-based care to improve the lives of individuals and families affected by HD.
Disclosure: This study is supported by F. Hoffmann-La Roche Ltd.

EPO-382

Cognitive functions in Meniere's disease

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Background and aims: The aim of this study is to investigate cognitive functions in Meniere's disease (MD).
Methods: We studied 29 MD patients (15F/14M aged 33–66) and 29 age and educationally matched healthy controls (HCs) (age range, 32–69). MD patients were divided into two groups: patients with persistent hearing loss and those with fluctuating hearing loss but normal hearing at the time of cognitive testing. Detailed neuropsychological tests for cognition and Hamilton Depression Scale were administered to all participants.
Results: MD patients showed mild impairment in general cognition, attention, verbal and visual memory, and executive function of moderate effect size compared to HC ($p<0.05$). MD with persistent hearing loss exhibited a decrease of large effect size in verbal visual and memory, and executive function compared to MD with normal hearing ($p<0.05$). Multiple linear regression analysis showed that depression scores had no effect in cognition ($p>0.05$). A statistically significant relationship was found between the presence and absence of hearing loss and attention ($r=0.428$, $p=0.020$), verbal memory ($r=0.617$, $p<0.001$), visual memory ($r=0.513$, $p=0.005$), and executive functions ($r=-0.493$, $p=0.007$) in MD patients.
Conclusion: Impairment in attention, verbal and visual memory, and executive functions was shown in MD. Hearing loss in MD contributes to impairment in verbal and visual memory, and executive function.
Disclosure: The authors report no conflicts of interest. All authors declared that they received no financial support.

EPO-383

Spontaneous microsaccades in amnestic and non-amnestic mild cognitive impairment

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Background and aims: This study aims to investigate measuring frequency of spontaneous "microsaccades" in mild cognitive impairment (MCI).
Methods: There were 20 patients with amnestic MCI (aMCI, mean age: 68±9) and nine non-amnestic MCI (naMCI, mean age: 68±8) and 24 healthy controls (HCs) (mean age: 64±10) in the study. The fixation task was presented as part of a battery of eye movement tasks using an Eyelink 1000 Plus eye tracker. Participants fixated a white spot (0.5°) on a black background displayed at the center of the monitor across two trials of 90 seconds each. Eye movement testing took place in a darkened room. Saccades were defined as any periods for which the instantaneous velocity exceeded 30° sec-1 with acceleration exceeding 3,000 ° sec-2. No minimum amplitude threshold was applied. Saccades were also classified as either large >0.5° or small <0.5°.
Results: Frequency of microsaccades (amplitudes <0.5 degree) was low in patients with aMCI compared to HCs (p=0.005). The mean amplitudes of microsaccades between 0.5–1.5 degrees were higher in patients with aMCI compared to HCs (p=0.001). Blink rates and pupil sizes were not statistically significant across groups.
Conclusion: In the present study, frequency of microsaccades and amplitudes were inconsistent across MCI patients and HCs. Future work could follow up MCI patients and HCs to determine whether any of them subsequently progressed to dementia and whether saccade measures discriminate between MCI and HCs.
Disclosure: The authors report no conflicts of interest. All authors declared that they received no financial support.

COVID-19 3

EPO-384

Thrombohemorrhagic brain damage in COVID-19 under the guise of Wernicke's encephalopathy

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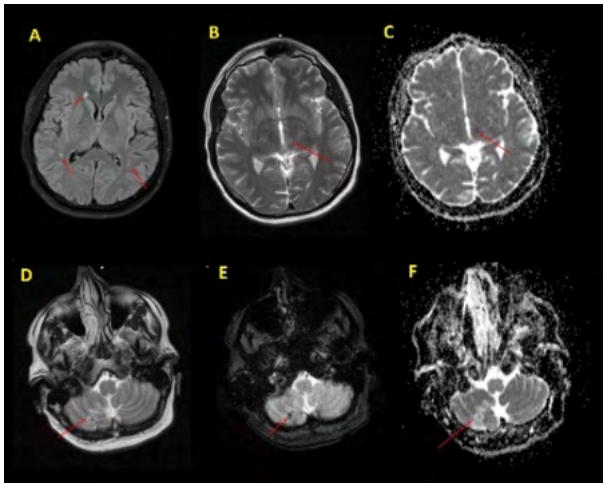
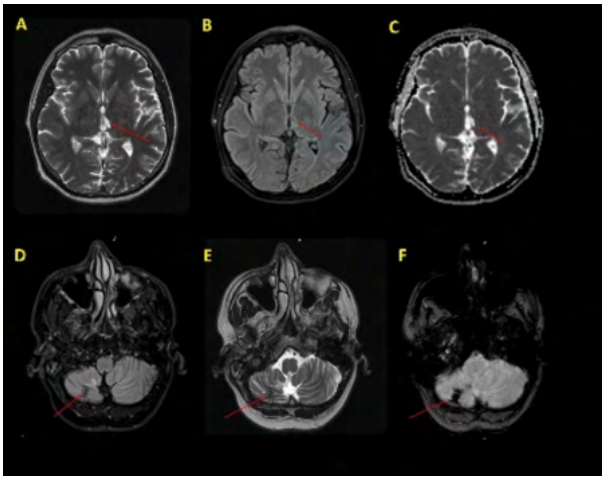
Background and aims: SARS-CoV-2 can cause different types of stroke.

Methods: We present two clinical cases of thrombohemorrhagic brain lesions in COVID-19, occurring under the guise of Wernicke encephalopathy.

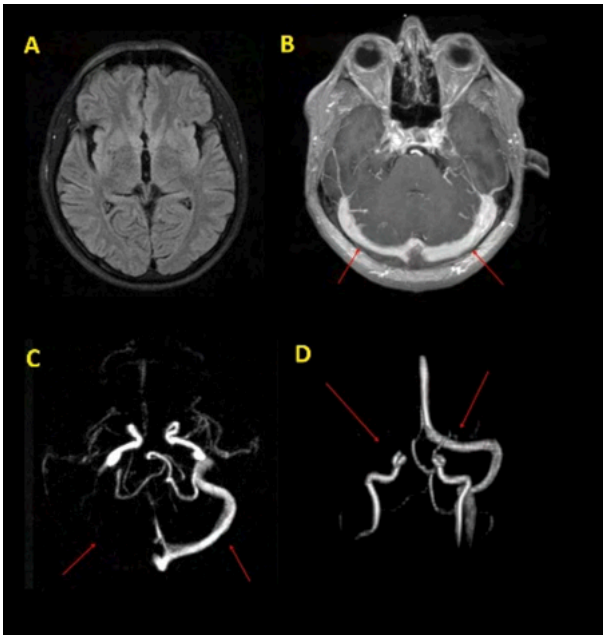
Results: Clinical case 1. 41-year-old patient got colitis, lost sense of smell . Then obtundation, bilateral ptosis, dysarthria were noted. On the 11th day, febrile fever was recorded. MRI revealed a lesion in the left thalamus, a lesion in the right hemisphere of the cerebellum with hemorrhagic impregnation. On the 27th day, pneumonia caused by SARS-CoV-2 was found. After four months, the patient had bilateral ptosis, vertical gaze palsy, divergent strabismus on the right, bilateral convergence palsy, internuclear ophthalmoplegia, mydriasis, ataxia, hyperactive tendon reflexes in the hands. linical case 2. A 43-year-old patient had a headache in the occipital region. A week later, the body temperature was 38 °C. On the 14th day, pneumonia was found. On the 21st day, the blood pressure was 180/130mm Hg, then it decreased to 100/60mm Hg, left-sided ptosis, strabismus, ataxia appeared. Diagnosed bilateral pneumonia was caused by SARS-CoV-2. Then new neurological symptoms developed. After two months, there was an episode of weakness in the left arm. Thrombosis of the right transverse sinus was found. Obviously, the cause of cerebrovascular disorders in patients was COVID-19. The diagnosed neurological disorders resemble the Wernicke encephalopathy.



MRI of the brain of the patient 1 on the 11th day from the onset of the disease. a – FLAIR mode, b – T2 mode, c – ADC map, d – T2 mode, e – T2 * mode, f – ADC map



MRI of the brain of the patient 1 after two months from the onset of the disease. a – T2 mode, b – FLAIR mode, c – ADC map, d – FLAIR mode, e – T2 mode, f – T2 * mode



MRI and MR-angiography of the brain of the patient 2 on the 25th (a,b) and 58th (c,d) days from the onset of the disease. a – FLAIR mode, b – T1 + C mode; c, d – data on MR venography

Conclusion: During the COVID-19 pandemic, doctors need to be alert to all patients with new-onset neurological symptoms. This will make it possible to diagnose COVID-19 in a timely manner.

Disclosure: The authors declare no conflict of interest. The study was performed without external funding.

Informed consent was obtained from all patients for being included in the study.

EPO-385

Analysis Of Delayed Admission to Hospital In Acute Stroke Patients During The Pandemic COVID-19 In Bishkek, Kyrgyzstan

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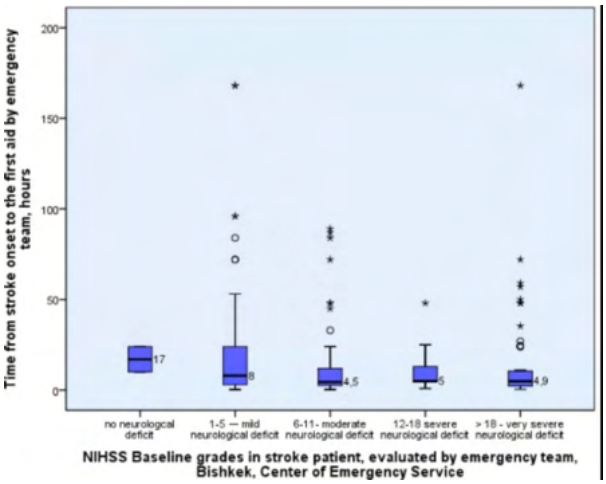
Background and aims: Stroke services worldwide experienced the drop and barriers in admissions of patients to acute stroke departments in COVID-19 pandemic time. We aimed to analyze how lockdown due to the pandemic affected the number of admissions of acute stroke.
Methods: Logistical parameters in 289 medical records of patients with acute stroke, examined by emergency teams of the Emergency Medical Center in Bishkek (EMCB) were analyzed retrospectively in four months in Bishkek, Kyrgyzstan: December 2019, January 2020 (prepandemic months) and July and August 2020 (highest COVID-infection rates).
Results: Only 50,1% of cases were recognised as "strokes" by the emergency dispatcher and the correct team was sent to the patient. The mean time from the stroke onset till emergency team arrival was 15.6±15.4 hours and the shortest median time (4.5 h) was in a group with the highest NIHSS score, p=0,01. In July 2020 (highest COVID infection rates in Kyrgyzstan) in 27.8% of cases an accepted stroke call was transferred by the dispatcher to the ambulance team within 90 minutes. 27.7% of stroke patients refused to be hospitalized in the pandemic time and in 8.3% of cases, patients were not hospitalized due to the lack of places in duty hospitals.



Median time after stroke onset till emergency services examination in different NIHSS grades in stroke patients in Bishkek

Conclusion: Prolongation in aid to stroke patients is caused with low stroke recognition by population, overload of emergency teams and patients refusal of the hospitalisation. COVID-19 pandemic in Kyrgyzstan though stimulated to train 91 emergency doctors in NIHSS and this scale was implemented in pandemic in prehospital settings.
Disclosure: Nothing to disclose.

EPO-386

A clinical case of Miller-Fisher syndrome after COVID-19

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Background and aims: Miller-Fisher syndrome (MFS) is one of the immune-mediated demyelinating polyneuropathies, which is observed in about 5% of all cases of Guillain-Barre syndrome. It presents as a triad of ataxia, areflexia, and ophthalmoplegia, but low frequency of generalized muscle weakness and bulbar palsy.
Methods: A 34-year-old male patient was admitted with a provisional diagnosis of ischemic stroke and the following symptoms: double vision, awkwardness in the right hand. Double vision, speech disturbances (dysarthria), weakness in the right hand has appeared one day before admission. In six hours speech and limb weakness were restored, but double vision began to deteriorate. Anamnesis of a moderate COVID-19 infection three weeks prior to symptoms onset. Brain MRI and MSCT were performed, features of stroke were not revealed.
Results: Neurological status: left side convergent squint, left and down gaze diplopia, weakness of convergence were detected; finger-nose-finger test revealed ataxia in the right hand, all deep reflexes were decreased D=S. Biochemical analysis of blood was normal. Lumbar puncture revealed elevation of protein (>0.95g/L) without an increase of lymphocytes Anti-myelin antibodies were detected (1:14).
Conclusion: MFS was diagnosed based on obtained data. Patient was successfully treated with Immunoglobulin G (35g per day for five days) with complete symptoms regression. Differential diagnosis with stroke, myasthenia gravis, other demyelinating disease was performed. A specialty of this case was the late development of the MFS after undergoing COVID-19.
Disclosure: Nothing to disclose.

EPO-387

Osmotic Demyelination Syndrome in a COVID-19 patient

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Background and aims: Accumulating evidence suggests that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) affects not only the respiratory tract, but also have neuroinvasive potential. The most common findings are cerebral ischemia and hemorrhages. Herein, we report a case of a 54-year-old woman with COVID-19 infection who developed a central pontine and extra pontine myelinolysis.

Methods: A 54-year-old female was admitted to the clinic for moderate pneumonia after a 10-day history of a non-productive cough, persistent fever and fatigue. Upper respiratory swab detected SARS-CoV-2 by PCR. T of the lungs showed ground-glass opacifications bilaterally. After admission she developed a headache, nausea and vomiting. Severe electrolyte disturbances were noted with a decrease in sodium levels to 103mmol/L (135–145mmol/L). After six days against the background of gradual normalization of sodium levels, the patient developed a seizure, became inadequate, agitated, stopped contacting the medical staff, did not answer questions. Lumbar puncture and brain CT were normal. A week later, the patient's condition worsened, dysphagia, severe tetraparesis, oculomotor disorders developed.

Results: MRI reveals T2/FLAIR hyperintensity involving the central brainstem with characteristic sparing of the periphery, typical of pontine myelinolysis (Fig.1) and extrapontine myelinolysis with symmetric lesions of the caudate and lentiform nuclei and partly the thalamus (Fig.2). Correction of sodium levels, pulse hormone therapy did not significantly improve the patient's condition.

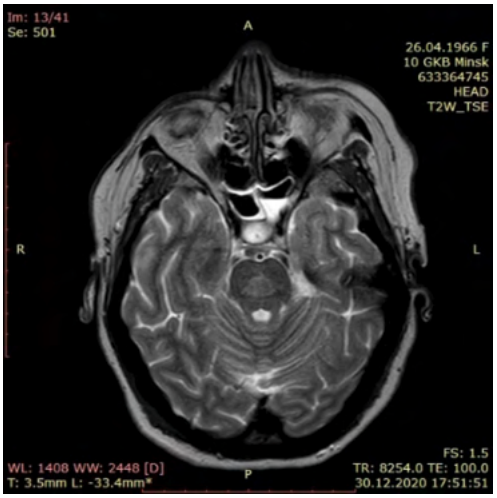

Fig.1 T2 axial image showing hyperintensity in central region of the pons suggesting central pontine myelinolysis.

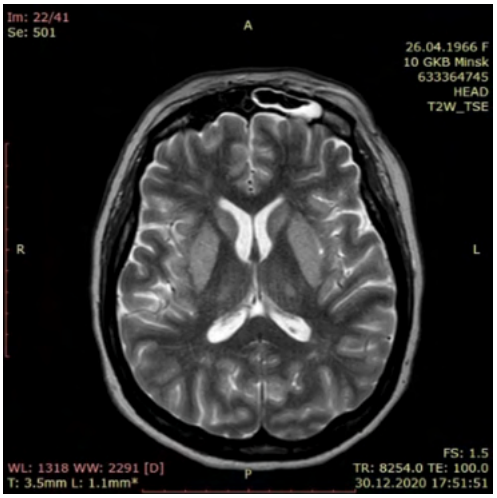

Fig.2 T2 axial image showing symmetrical hyperintensities in caudate and lentiform nuclei and also partly the thalamus consistent with extrapontine myelinolysis.

Conclusion: The presented case shows that hyponatremia can be a disorder associated with COVID-19 and may lead to osmotic demyelinating syndrome, which requires more frequent monitoring of sodium levels in patients with COVID-19.

Disclosure: Nothing to disclose.

EPO-388

COVID-19 and stroke at Yaounde General Hospital

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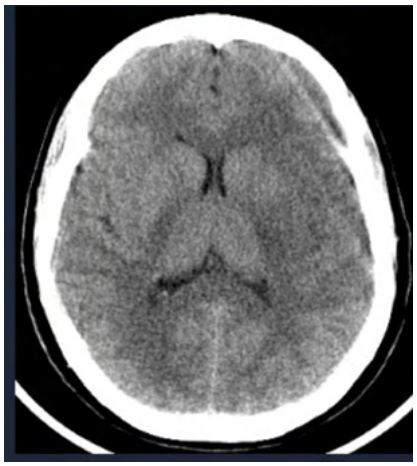
Background and aims: COVID-19 infection causes serious damage to the respiratory system, but several studies have reported neurological damage with different manifestations known as: "NeuroCovid".
Methods: It was a prospective study in Yaounde General hospital during three months. We included all the patients who had stroke, and a positive test to COVID-19, with a neuro-imaging sign.
Results: We report five patients who were infected with Covid 19 and who had an Ischemic Stroke. 80% were diagnosed with COVID-19 infection at the same time as a stroke in the emergency room, and one patient presented with signs of stroke approximately 10 days after being diagnosed with COVID-19 infection. Among our patients we found four men and one woman, all were aged above 38 years, and the oldest was 59 years old. Cardiovascular history (high blood pressure, diabetes, atrial fibrillation) was present in three patients. Ischemia in the territory of the left middle cerebral artery was found on ct-scan for 80% of them, and 2/5 developed an aphasia. The evolution was favorable with good motor recovery for two of them and severe motor sequelae for other 3.



Early ischemic stroke of the left middle cerebral artery

Conclusion: COVID-19 pandemic is a global reality with multiple consequences, several systems are involved, including the central nervous system and ischemic stroke is a well-described complication
Disclosure: Accepted. No conflict of interest

EPO-389

Total cervicothoracic myelitis in a patient with severe COVID-19 pneumonia

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Background and aims: Patients with COVID-19 infection may have neurological complications, some of which can be rapidly progressing, requiring urgent intervention.
Methods: Case report of acute myelitis in a COVID-19 patient.
Results: A 49-year-old man, previously diagnosed with SARS-Cov2-infection, was admitted into the emergency department (ED) with a 3-day history of severe ascending bilateral weakness. On day five of his COVID-19 symptoms, he developed low back pain, lower limb paresthesia, and bilateral lower limb weakness, which progressed to severe quadriparesis with urinary retention over the next two days. There was no history of trauma, fever, preceding diarrhoea, or recent vaccination. Preliminary evaluation in the ED revealed respiratory failure with an increasing requirement for respiratory support. On neurological examination, he had flaccid quadriparesis, with severe lower limb weakness; hyperreflexia with ankle clonus and bilateral Babinski signs; bilateral T8-sensory level; and impaired proprioception of the lower limbs. Thoracic CT confirmed COVID-19 pneumonia. MRI scan of the whole spine showed T2 hyperintensity, extending from the cervicomedullary junction to T12 and involving more than two-thirds of the spinal cord transverse section, with associated diffuse enhancement. CSF examination revealed a lymphocyte-predominant pleocytosis (90/L) with moderately elevated protein (1.08g/L) and normal glucose. Laboratory studies, including aquaporin-4–IgG and myelin-oligodendrocyte glycoprotein-IgG, were normal. He was admitted to the intensive care unit for ventilatory support and treatment with remdesivir and IV methylprednisolone was initiated.
Conclusion: To our knowledge, this is the case with the most extensive myelitis reported in association with COVID-19 infection. We aim to highlight it and discuss its potential pathogenic mechanisms.
Disclosure: Nothing to disclose.

EPO-390

Impact of the COVID-19 pandemic on the stroke cases notification in Brazil

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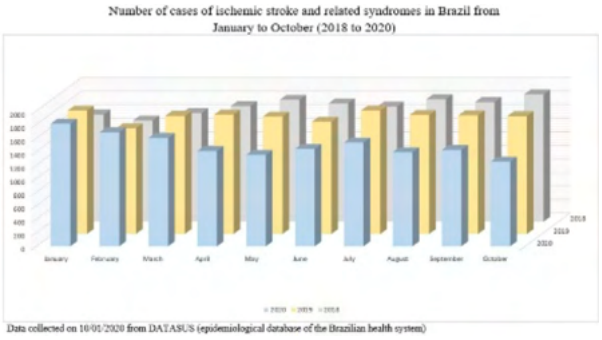
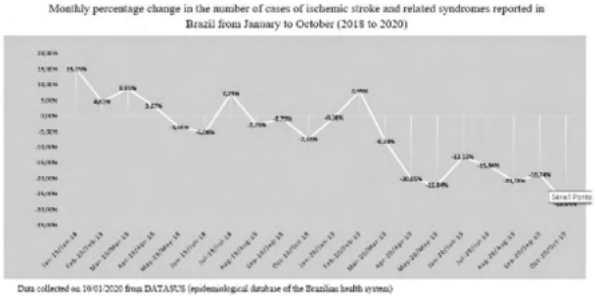
Background and aims: The Coronavirus Disease Pandemic – 2019 (COVID-19) represents, to date, the greatest public health challenge of the 21st century. Stroke, on the other hand, is nationally the main cause of disability, accompanied by a considerable and costly number of hospitalizations. This paper questions the impact of COVID-19 on stroke notifications.

Methods: Articles were searched using the descriptors: Ischemic Stroke; Hemorrhagic Stroke; Cerebrovascular events; COVID-19 and Brazil. The research platforms were Pubmed, Scielo, Virtual Health Library and DataSUS.

Results: Since the beginning of the pandemic in Brazil, in March 2020, there has been a reduction of approximately 20% in the number of stroke cases reported compared to 2019. This reality is consistent with the international scenario of possible underreporting and reduced demand for medical care in mild and intermediate cases. Although, according to medical societies of national specialties, COVID-19 does not change the recommendations for the management of patients with stroke, the result of this context may be a late start of care, loss of the therapeutic window and worsening of stroke outcomes in the country. The attention to safety protocols and the importance of telemedicine for pre-hospital care was also highlighted.





Conclusion: Given the decrease in the number of cases of stroke, there is an alert regarding underreporting and delay in care, problems already present in the national scenario that may be potentiated by the pandemic, where the concern with COVID-19 overlaps with other diseases, which may increase the damage (in the short and long term) to public health.

Disclosure: Nothing to disclose.

EPO-391

Reversible encephalopathy following mild respiratory symptoms of COVID-19

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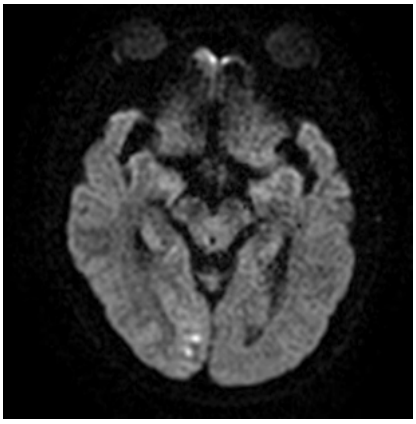
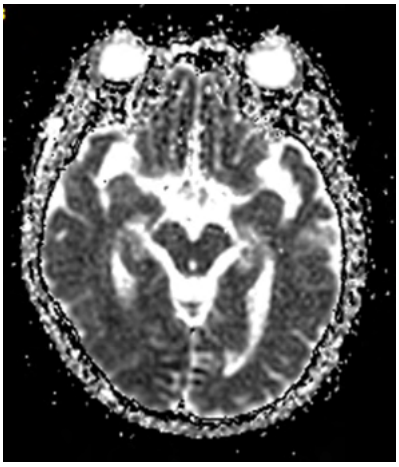
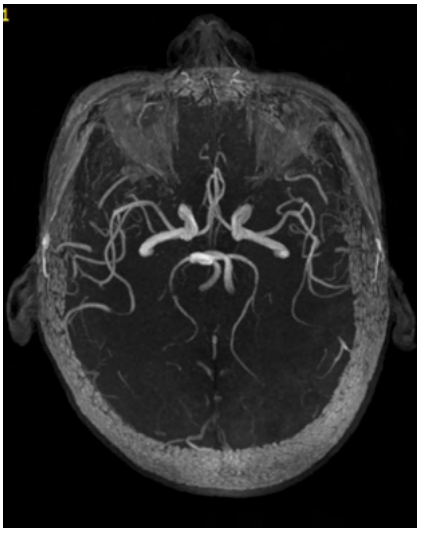
Background and aims: Diverse neurologic symptoms in patients with COVID-19 have been reported. Encephalopathy usually develops in association with severe COVID-19. We present the case of a transient encephalopathy following mild respiratory symptoms of COVID-19.
Methods: Case report.
Results: 56-year-old male came to our attention because of headache and altered vision. His neurological examination on admission revealed visual anosognosia. Two weeks before the onset of neurological symptoms, he developed mild COVID-19 respiratory tract infection. His medical history included recently diagnosed type 2 diabetes mellitus on metformin and gliclazide treatment. An acute CT scan of the head was normal. A CT angiography showed stenosis of a right posterior cerebral artery. Antiplatelet therapy was started. The 2nd day after admission, the patient developed confusion and recurrent brief episodes of head and eye deviation to the left with impairment awareness. The 1st-line antiepileptic treatment with i.v. valproate was not fully effective. Some seizure control was achieved after adding benzodiazepines to his treatment. The 3rd day after admission, brain MRI revealed subtle subcortical ischemic changes in the right occipital lobe, stenosis of posterior cerebral artery, and T2 and FLAIR hyperintensities within the right hippocampus consistent with ongoing seizure activity. Over the next few days, antipsychotics were used to treat delirium. Recurring seizures were controlled after lacosamide was started. On the seventh day after admission, our patient was mildly confused but fully cooperative. His visual field testing field revealed no abnormality.



MRI - DWI: ischemic changes in the right occipital lobe



MRI - ADC: ischemic changes in the right occipital lobe



MR angio: stenosis of a right posterior cerebral artery.

Conclusion: Reversible encephalopathy can follow mild respiratory symptoms of COVID-19.
Disclosure: Nothing to disclose.

EPO-392

Chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids (CLIPPERS) after COVID-19

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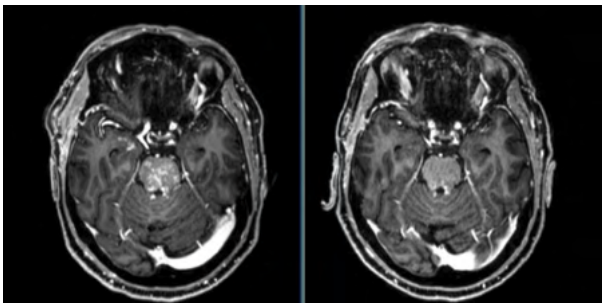
Background and aims: SARS-CoV-2 infection is now known to be associated with a wide spectrum of neurological autoimmune syndromes, in some cases responding to immunotherapies, arising during or after the infection. Whether molecular mimicry or other immune stimulation may induce an aberrant delayed autoimmune response is still to be established.

Methods: Case report.

Results: A 71 year-old man with no previous medical history apart from mild COVID-19 pneumonia three month earlier, sought medical attention for a subacute onset of diplopia in left gaze, general malaise and fatigue. MRI was characterized by bilateral FLAIR hyperintensities with punctate, perivascular and confluent post-gadolinium enhancement in the pons, mesencephalon, hypothalamus, internal capsules and right hippocampus. Repeated cerebrospinal fluid analysis were normal (2 cells/μL), with no evidence of oligoclonal bands or atypical cells. Screening panel for autoimmune and infectious aetiologies was negative. Whole-body contrast-enhanced CT was unremarkable. Stereotactic temporal lobe brain biopsy showed aspecific chronic lymphocytic perivascular inflammation. Partial spontaneous remission of symptoms occurred within few weeks. He was then treated with intravenous high-dose methylprednisolone with almost complete enhancement regression on MRI. Collected data were suggestive of CLIPPERS with diffuse bilateral sovratentorial involvement. The patient started daily oral steroid tapering and monthly cycles of intravenous cyclophosphamide with persistent clinical and neuroradiological stability.



Contrast enhancement disappearance on T1 weighted MRI scans after corticosteroid treatment

Conclusion: CLIPPERS is a rare diagnosis and to the best of our knowledge, this is the first time it was reported after COVID-19 disease. Even though a case report is not enough to suggest a causal link, future reports could support this possibility.

Disclosure: Nothing relevant to the present study.

EPO-393

Impact of the COVID-19 lockdown in Multiple Sclerosis patients

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Background and aims: The COVID-19 pandemic persisting crisis showed an upheaval on the whole world. People with multiple sclerosis (MS) are a particularly vulnerable group. We aimed to assess how this pandemic has affected MS patients during the lockdown decreed in Tunisia.
Methods: After obtaining the approval of ethics committee, a phone survey was conducted from the 15th of May to the 15th of June in the MS center in Razi hospital in Tunis-Tunisia. The designed questionnaire includedin particular the impact of the lockdown on patients' medical follow-up, MS symptoms, treatment availability and daily lifestyle and professional activities.
Results: A total of 213 questionnaires were fulfilled. There was no SARS CoV-2 infected case in our cohort. Patients completely followed quarantine guidelines in 176 cases (82.6%). Professional activities were totally stopped in 80.3% while teleworking was adopted in only 4.9% of active patients. During the lockdown, 46 patients (21.6%) experienced a relapse. Steroids were prescribed in 15 cases. Exacerbation of existing symptoms related to MS was described by 133 patients (mainly mood disorders (87%) and sleep disturbances (62%)). About 58 patients interrupted their MS treatments mainly because of mobility issues (n=24) and treatment unavailability (n=27). This was significatively associated with the exacerbation of neuropathic pain (p=0.01)) but not with relapses (p=0.27). Physical activity interruption was associated to the exacerbation of fatigue (p=0.02).
Conclusion: COVID-19 lockdown negatively affected our MS patients especially in work, psychological state and MS treatments availability. As a consequence, worsening of MS related symptoms and psychiatric features were described.
Disclosure: Nothing to disclose.

EPO-394

The COVID-19 pandemic disproportionately disrupts neurology and related fields in Cluj county

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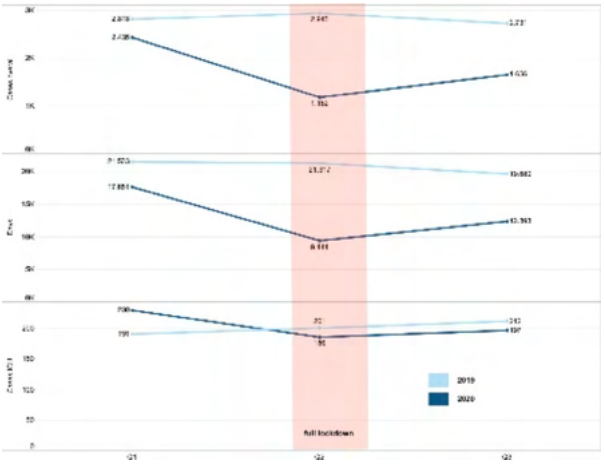
Background and aims: SARS-CoV-2 has forced countries to enter into lockdown to contain the community spread of the virus. Mobility of Romanian patients has been strongly restricted ever since. Even during a pandemic, access to care for chronic or acute neurological conditions such as stroke and to surgical or pharmacological treatment is crucial to prevent disastrous health outcomes. Given the overall scarcity of information regarding the pandemic's impact on non-COVID-19 care in lower resource countries such as Romania, we set out to compare quarterly volume indicators for a selection of neurology-related wards.
Methods: The total number of inpatient and outpatient cases, hospitalization days, and intensive care unit (ICU) cases reported in neurology, pediatric neurology and neurosurgery wards in Cluj county, Romania, were retrieved from a publicly available database comprised of private and public hospitals engaged in service provision contracts with the Romanian National Health Insurance House.
Results: In comparison with 2019, Cluj County reported between 14–60% fewer quarterly cases and 18–56% fewer hospitalization days (Table 1). During the first quarter of 2020, ICU cases rose by 20% compared to the previous year. The third quarter of 2020 shows a slight improvement in all indicators (Figure 1), despite a 75% increase in neuropediatric ICU cases. Out of all studied specialties, neurosurgery was least impacted.

Ward	Indicator	Quarter 1 2019	Quarter 1 2020	Quarter 1 % Difference	Quarter 2 2019	Quarter 2 2020	Quarter 2 % Difference	Quarter 3 2019	Quarter 3 2020	Quarter 3 % Difference
Neurology	Days	14.388	11.432	-19,85%	13.940	5.890	-59,20%	12.809	7.415	-42,10%
	Cases overall	1.742	1.548	-11,25%	1.782	669	-61,55%	1.705	926	-45,86%
	Cases ICU	86	94	-7,08%	81	60	-26,03%	91	77	-15,38%
Neurosurgery	Days	5.525	4.939	-10,57%	5.444	3.059	-44,18%	5.568	4.327	-24,95%
	Cases overall	582	563	-3,36%	627	327	-47,85%	608	495	-17,33%
	Cases ICU	75	118	57,33%	112	114	1,79%	113	106	-6,19%
Pediatric Neurology	Days	1.922	1.283	-33,40%	1.928	710	-62,91%	1.008	95[illegible]	-36,94%
	Cases overall	514	329	-35,99%	526	166	-68,44%	419	231	-44,74%
	Cases ICU	20	18	10,00%	8	12	50,00%	8	14	75,00%
Grand Total	Days	21.535	17.651	-18,03%	21.317	9.444	-55,70%	19.680	12.36[illegible]	-37,03%
	Cases overall	2.818	2.435	-13,59%	2.945	1.162	-59,66%	2.731	1.656	-39,36%
	Cases ICU	181	230	20,42%	201	186	-7,46%	212	197	-7,08%

Quarterly differences in hospital care volume indicators, before and during the COVID-19 pandemic



Overall trends across first three quarters of 2019 and 2020

Conclusion: Based on this pilot analysis, we assert that key specialties treating high-burden diseases such as neurology, pediatric neurology, and neurosurgery are disproportionately disrupted by the COVID-19 pandemic. National authorities should conduct active surveillance of this issue.
Disclosure: Nothing to disclose.

EPO-395

Covid-19 Associated Severe Encephalopathy

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Department of Neurology, Istanbul, Turkey

Background and aims: A growing body of literature suggest a broad spectrum of central nervous system(CNS) manifestations associated with COVID-19.Encephalopathy and encephalitis are major and devastating SARSCoV2-virusassociated CNS complications.Herein, we report a case with severe COVID-19-related encephalopathy.

Methods: A-45-years-old healthy man,admitted to emergency room with nausea,vomiting,diarrhea,altered consciousness. Nasopharyngeal swab was positive for Covid-19 and he was on plaquenil treatment since two days. Neurological examination revealed left hemiparesis and altered consciousness.Chest computed tomography showed,there were ground glass opacities on both sides of inferior lobes compatible with Covid-19 pneumonia (Figure-1). His serum sample was positive for anti-SARS-CoV-2-IgG. Brain magnetic resonance (MR) imaging studies demonstrated an hyperintense lesion in T2 and FLAIR-weighted series with subtle contrast enhancement in right frontoparietal region with a mass effect (Figure-2). MR-spectroscopy was consistent with evidence of leukoencephalopathy and inflammation. He was treated with plaquenil,favipiravir and dexamethasone 32mg/daily. His neurological impairment worsened and there was progression on brain MR lesion (Figure-3). He was intubated and mechanically ventilated for COVID-19-related respiratory distress syndrome and impaired consciousness. He received immunotherapy combining corticosteroid infusions (1g/day intravenous methylprednisolone for two days)initially and then plasma exchange with albumin (2 sessions).

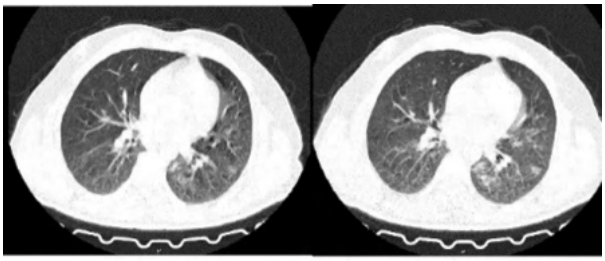

Figure-1

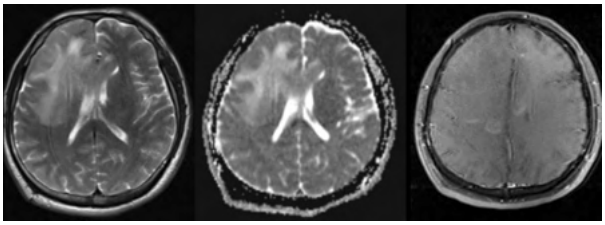

Figure-2

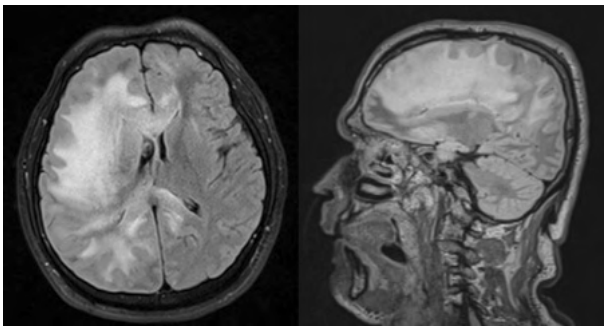

Figure-3

Results: It is worth noting that neurological impairment remained unchanged.On the tenth day of hospitalization,the patient developed cardiopulmonary arrest and died.

Conclusion: This report indicates that CNS may be involved in COVID-19 and mentions the importance of diagnostic and therapeutic approaches to SARS-CoV-2 associated encephalopathy.The pathophysiological characteristic is not fully understood.An immune-mediated mechanism has been proposed to explain corona viruses associated encephalitis.However,encephalitis has seldom been reported and the potential benefit of immunotherapy remains unclear.

Disclosure: Nothing to disclose.

EPO-396

Risk factors of hemorrhagic stroke associated with COVID-19

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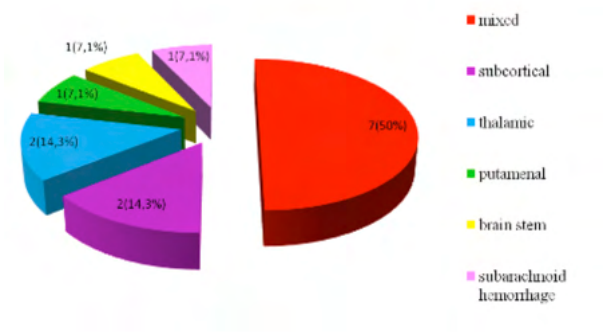
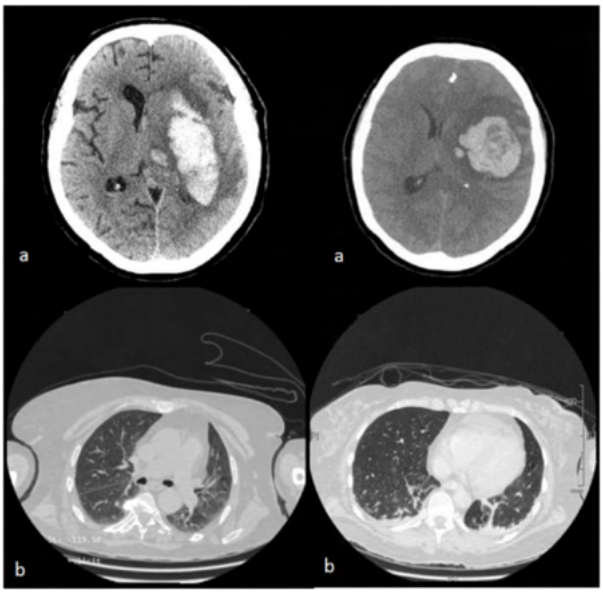
Background and aims: Acute stroke is a highly specific neurological symptom in the acute phase of COVID-19 infection. The risk of hemorrhagic stroke (HS) in patients with COVID-19 in Wuhan (China) according to Yanan Li et al and Ling Mao et al (2020) studies was 0.5% and 1.1%, respectively. **Purpose:** analysis of risk factors for HS associated with COVID-19.

Methods: 100 case histories of patients with stroke associated with COVID-19 in the vascular center (COVID-19-hospital) in Ufa were studied. 14 (14%) of them with HS. The diagnosis was established on the basis of clinical, instrumental, laboratory and neuroimaging examinations. Data processing was carried out using Statistica 6.0.

Results: The average age of patients was 65.3±9 years. By gender, the ratio is 1:1. 3(21.4%) patients had recurrent stroke. The localization of intracerebral hematomas and neuroimaging data are presented in pic. 1 and 2. Hematomas of mixed localization prevailed (50%). The average volume of hematomas was 26.4±18.3cm^3. On admission, 13(92.9%) patients had a viral pneumonia with typical CT signs of "ground glass". Severe pneumonia was observed in 6(42.9%) patients. In 4(28.6%) patients, SARS-CoV-2 was identified by PCR. All patients had concomitant somatic pathology: hypertension 14 (100%), heart disease 4(28.6%), kidney disease 4(28.6%), liver disease 3(21.4%), malignant tumor 2(14.3%), chronic alcoholism 2(14.3%). Laboratory parameters are shown in table 1. All patients had coagulopathy (100%). 11(78.6%) cases were fatal.



Pic.1. Localization of intracerebral hematomas.



Pic. 2. a. Computer tomography of the brain. b. Computer tomography of the lungs

Indicators	n (%)	Indicators	n (%)
Coagulopathy (total)	14(100%)	Lymphocytopenia	13(92.9%)
The combination of hypo and hypercoagulation	3(21.4%)	Monocytopenia	7(50%)
Hypercoagulation	8(57.1%)	High C-reactive protein	8(57.1%)
Hypocoagulation	3(21.4%)	High D-dimer	6(66.7%)
Hyperfibrinogenemia	8(57.1%)	High creatinine	6(12.9%)
High activated partial thromboplastin time	7 (50%)	High urea	7 (50%)
Hyperglycemia	10(71.4%)	Low hemoglobin	5(35.7%)
Dyslipidemia	6(42.9%)	High alanine aminotransferase	3(21.4%)
The partial pressure of O2 below normal	6(42.9%)	High aspartate aminotransferase	12(85.7%)
Partial pressure of CO2 above normal	4(28.6%)	High total bilirubin	5(35.7%)
Neutrophil leukocytosis	9(64.3%)	High creatine phosphokinase	8(57.1%)
Thrombocytopenia	9(64.3%)	High lactate dehydrogenase	11(78.6%)

Table 1.Laboratory data.

Conclusion: The leading etiopathogenetic factors of HS were hypertension, coagulopathy, hyperglycemia, thrombocytopenia, renal-hepatic insufficiency, high C-reactive protein. The COVID-19 pandemic requires further in-depth study for effective patient care.

Disclosure: Nothing to disclose.

EPO-397

Acute Disseminated Encephalomyelitis in Adults with COVID-19: Case Report and systematic review of the literature

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Background and aims: Acute disseminated encephalomyelitis (ADEM) is a neurological autoimmune disease that usually occurs after a systemic infection, mostly viral. It is not clear the association between ADEM and SARS-CoV-2 infection. Therefore, we performed a systematic review of worldwide reported cases to qualitative describe this relationship; additionally, we present a patient with SARs-CoV-2 infection who then developed ADEM.
Methods: A systematic search in Pubmed/MEDLINE, Embase, and LILACS was conducted (until November 29, 2020) following the PRISMA guidelines. We included published case reports of adult patients reporting narrative and descriptive data per case report. We used a meta-synthesis approach to summarize the available evidence, in addition to one case report from our hospital (figure 1).
Results: We included 18 cases. We observed male predominance with a mean age of 53 years old. The mean number of days from COVID-19 infection to ADEM diagnosis was 22.2 days. Regarding COVID-19 severity, 70.6% were severe, 17.6% mild, and 11.8% asymptomatic. The most common clinical characteristics were encephalopathy (81.3%) and pyramidal signs (68.8%). In MRI, all presented white matter compromise, and 44.4% brainstem lesions. The most frequently described alteration in the CSF was hyper proteinorrachia (mean: 63.1mg/dL). two cases died and 16 cases responded partially to corticosteroid treatment.

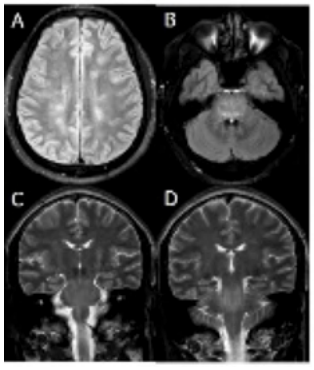

Figure 1. A. T2-weighted axial MRI / FLAIR shows multiple bilateral hyperintense flocculating lesions in the white matter of the semioval center and corona radiata. B. T2-weighted axial MRI / FLAIR shows hyperintense lesions in the bilateral pontine tegme

Conclusion: Patients with different COVID-19 severities (even asymptomatic) could develop ADEM. Neurologists must be alert to the occurrence of multifocal neurological symptoms associated or not with encephalopathy in patients recovered from severe COVID-19 disease. Timely MRI studies should be performed to establish the diagnosis and considering early corticosteroid-based treatment.
Disclosure: No conflict of interest.

EPO-398

Facial Diplegia as a variant type of Guillain-Barré Syndrome (GBS) related to COVID-19

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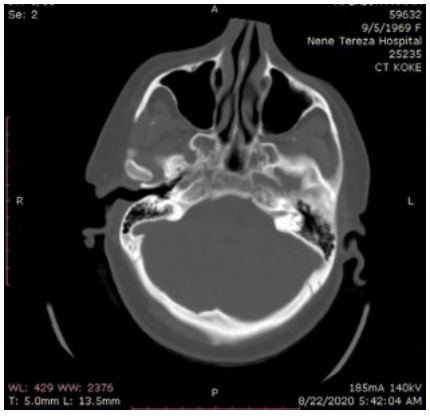
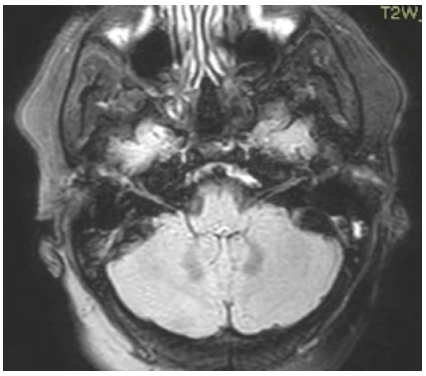
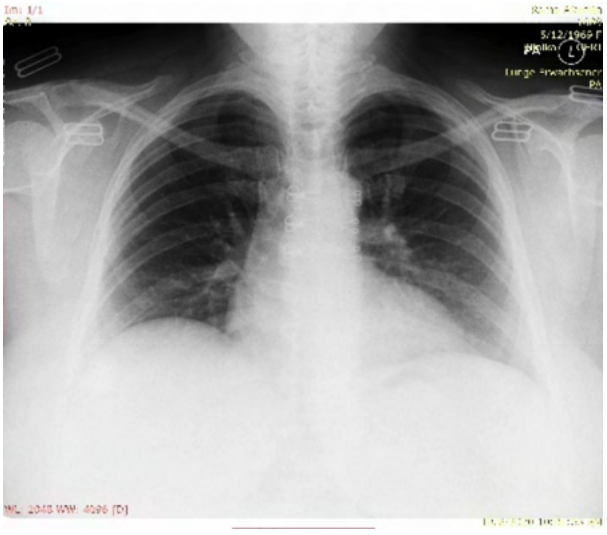
Background and aims: Several case reports published recently have attributed numerous neurologic complications to the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Guillain-Barre syndrome (GBS) and its variants, including facial diplegia are among some listed neurologic complications of COVID-19. In the background of the current COVID-19 pandemic a patient with Facial Diplegia related to acute inflammatory demyelinating polyneuropathy (AIDP) should be regarded as having a preceding or actual SARS-CoV-2 infection.
Methods: We present the case of a patient with facial diplegia following a SARS-CoV-2 infection without prior relevant clinical history, managed conservatively with a favorable outcome. It is important to consider SARS-CoV-2 infection a potential trigger of AIDP, in cases presented with bilateral peripheral facial nerve paralysis. A high clinical suspicion will prompt to immediate management of these patients who will benefit from therapeutic management and hospitalization.



Axial CT/Bone window Pontocerebellar angles and internal acoustic channels with normal aspect.



Axial FLAIR MRI shows normal signal of CN's VII and VIII.



Chest X-ray shows basal bilateral diffuse opacities

Results: GBS can be the presenting disorder that evokes a diagnosis of a precedent COVID-19. Although the patient was asymptomatic from a respiratory perspective, her positive SARS-CoV-2 serological tests along with clinical-electrophysiological findings were indicative of an antecedent SARS-CoV-2 infection directly responsible for the neurological complication.
Conclusion: These results should be seen with careful adjustments and warrants future investigation since the knowledge of the pandemic of SARS-CoV-2 infection is rapidly changing. On the other hand our case adds on to those few other reported cases in the literature with the distinguishable feature of total neurological signs resolution with corticosteroid therapy.
Disclosure: No financial disclosures.

Epilepsy 3

EPO-399

Issues of tissue metabolomics and histoproteomics in pharmacoresistant epilepsy

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Background and aims: The study of histoproteomics and tissue metabolomics in pharmacoresistant epilepsy continues to be a pressing problem for specialists of various fields.
Methods: We examined biopsy material from 32 operated patients with focal temporal lobe epilepsy that was pharmacoresistant. Hematoxylin-eosin and Spielmeier stains (for myelin, sudan for fat) were used. In some cases, electron microscopy was performed. The content of glycolipids and phospholipids, which are characteristic components of nerve cell membranes, was determined. Lipids were extracted from brain tissue using the "chloroform-methanol" mixture by the Folch method.
Results: Was performed immunohistochemical reactions with antibodies to CD45 (leukocyte common antigen), CD3 (T-lymphocytes), CD8 (T-killer cells, whose presence indicates active inflammation), CD20 (B lymphocytes), CD68 (macrophages) (DAKO, Denmark). Expression of CD3 was determined in 65%, CD8 – in 20% , CD20 – 6% , CD68 – 9% . In every case (100%) patients with Epilepsy revealed the expression of caspase-3 in gliocytes with predominant localization in the cortex of the temporal lobe. The expression of caspase-3 in neurons has been detected in 20% of observations in single cells. In the comparison group, the expression of caspase-3 was observed only sporadically in a cortical gliocytes. Using electron microscopy we identified a large number of neurons in the cortex with signs of apoptosis at different stages of this process' development. Apoptotic changes in glial cells were predominantly observed in oligodendrocytes both in the cortex and white matter of the brain.
Conclusion: Glio-neuronal apoptosis and neuroinflammation in focal pharmacoresistant epilepsy have a pronounced manifestation, and this affects the progression of the disease.
Disclosure: The study was carried out with the financial support of the RFBR Grant No. 20-015-00127.

EPO-400

Morphological findings in structural pharmacoresistant focal temporal lobe epilepsy in adult patients

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Background and aims: The study of morphological findings in structural focal pharmacoresistant epilepsy is an urgent task in the course of solving conceptual questions of epileptogenesis.
Methods: We examined biopsy material from 67 operated patients aged 19 to 53 years with focal temporal lobe epilepsy, which was pharmacoresistant. In all cases, histological examination of tissue removed during surgery and immunohistochemical methods were performed. In some cases, electron microscopy was also performed.
Results: A total of 67 patients aged 19 to 53 years with structural pharmacoresistant temporal lobe epilepsy were examined and operated on. Focal cortical dysplasia (FCD) detected in 12 patients. In four cases, mesial temporal sclerosis (MTS) occurred. Changes of glia in foci of epileptogenesis deserve special attention. Clinical and morphological comparisons revealed that patients with a severe course of the disease (and sometimes with a history of epileptic status) had a very mild astrocytic reaction with the presence of foci of demyelination in the cortex and subcortex. On the contrary, in patients with a milder course of epilepsy, without a history of epileptic status, glial reactions were very pronounced.
Conclusion: The changes detected in the cortex and white matter of the temporal lobe of the brain in the examined patients will allow us to clarify some questions of the epileptogenesis. According to our studies, astrocytic gliosis in the foci of epileptogenesis in structural pharmacoresistant focal temporal lobe epilepsy is not pathological, but an adaptive (protective) reaction.
Disclosure: The study was carried out with the financial support of the Russian Foundation for Basic Research (RFBR) Grant No. 20-015-00127.

EPO-401

An implantable sub-scalp electroencephalography device for the recording of epileptic seizures – a case study

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Background and aims: The objective of this case report is to present preliminary findings of an implantable sub-scalp EEG device (Minder) for recording epileptic seizures.
Methods: A 50-year-old female with epilepsy (subependymal nodular heterotopia), who reported 20 seizures per month at enrolment, was implanted with Minder device, consisting of an implantable telemetry unit and two-channel electrode. A wearable behind-ear device, mobile phone and cloud storage were used to capture continuous long-term EEG. Minder was evaluated for safety by collecting all adverse events. A patient witness seizure diary was used to report seizures throughout the study. "Gold standard" 7-day inpatient video-EEG using International 10-20 system were performed at 4- and 24-weeks post-implantation. EEG were independently reviewed by two blinded epileptologists. Discordance was resolved by a third epilepsy specialist. Minder EEG was also reviewed as per routine clinical practice, but prior to video-EEG to ensure measurement bias favours video-EEG. The two conventional modalities of seizure detection were compared against Minder to evaluate accuracy.
Results: Minder recorded continuous EEG signals throughout the 13 months. Minder accurately identified all seizures seen during the video-EEG. When compared to the seizure diary, six of seven reported events were confirmed to be seizure clinically and on EEG. The Minder confirmed an additional 18 patient unreported seizures detected on standard video-EEG recording. No serious device related adverse event occurred, the patient reported the device was comfortable and was able to use it both day and night.
Conclusion: This case report demonstrated that Minder is feasible, safe and acceptable for seizure monitoring in patients.
Disclosure: Some of the authors declare that they have personal financial interests.

EPO-402

Usher syndrome type II and epilepsy, coincidence?

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Background and aims: Usher syndrome is an autosomal recessive disease, clinically and genetically heterogeneous, characterized by moderate to severe congenital sensorineural deafness and progressive pigmentous retinitis, beginning in late adolescence or young adulthood. Of the three known types, type II is the most common and these patients do not have any vestibular dysfunction.
Methods: Case report
Results: A 30-year-old male with mild bilateral sensorineural deafness and pigmentary retinitis, which began at the age of 12 and 15 years, respectively, was recently diagnosed with Usher syndrome type IID after identification of a homozygous variant in the WHRN gene through complete genome sequencing. He was initially observed in the emergency room for an unwitnessed episode of loss of consciousness and then referenced to the neurology consultation. There, he described experienced paroxysmal episodes of language deficits, without prodromes, loss of consciousness or automatisms that would last one to two minutes. Brain magnetic resonance imaging showed an incidental finding of right retrocerebellar cyst, without other abnormalities. The electroencephalogram revealed an independent bilateral frontotemporal epileptiform discharge, activated by drowsiness and sleep, with slow intermittent temporal activity more frequent on the left side. He is seizure free following initiation of levetiracetam.
Conclusion: Usher syndrome is a rare disease without a clear known association with epilepsy. Despite the likely coincidence, this case aims to alert to the possible association, based on the fact that the causal gene for Usher syndrome type IIC is also found in patients with familial febrile seizures.
Disclosure: The authors do not have any conflicts of interest to declare.

EPO-403

EG findings in patients with COVID-19 infection and impaired consciousness

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Background and aims: One fifth of patients with COVID-19 may develop neurological symptoms. High rates of electroencephalographic (EEG) abnormalities were reported patients with SARS-CoV-2 infection and altered mental state. The aim of this study was to review the EEG findings in Polish patients with impaired consciousness and COVID-19 infection.
Methods: We retrospectively reviewed medical records and EEG studies of patients with COVID-19 infections and impairment of consciousness hospitalized in 2020 in University Hospital in Kraków.
Results: We analyzed 23 EEG performed in 18 patients, 61% (11) were females (median age 62,3 years). SARS-CoV-2 infection was the main cause of hospitalization in only 11,1% subjects. The remaining patients were hospitalized due to neurological disorders. Clinically significant MR or CT scan were found in 10 patients (55,56%) and CSF abnormalities in 7(38,8%). 14 (77,78%) patients took psychoactive drugs at time of EEG: 9(50%) took antiseizure medication and 5(27,78%) psychiatric drugs. EEG was normal in three (13%) patients. The most frequent EEG finding (9; 39,13%), was generalized slowing in theta/delta range. Focal slowing was found in two patients. Epileptiform discharges were present in three (16,67%) patients and five (21,7%) EEG. Seizures were recorded in three EEG (13,04%), focal status epilepticus in 2 EEG (8,7%). Among patients with epileptiform discharges 2(75%) had a history of epilepsy/seizures, 1(25%) had abnormalities in neuroimaging (changes specific to PRES) and 1(25%) had elevated level of cytosis (7 cells) in CSF.
Conclusion: Abnormal background activity is common in COVID-19 and altered mental status. The majority of patients with epileptiform discharges have a history of epilepsy/seizures.
Disclosure: Nothing to disclose.

EPO-404

The impact of maternal seizures on delivery outcomes

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Background and aims: The aim of the study was to assess the impact of seizures in pregnant women with epilepsy (WWE) on adverse delivery outcomes.
Methods: We prospectively evaluated 112 pregnant women with epilepsy for the period from April, 2013 to February, 2018. The obstetric outcomes for WWE were compared with those for 277 healthy women in control group.
Results: The mean age in study group was 24.8±0.4 years, in control group was 24.3±0.2. The average duration of epilepsy at the time of pregnancy was 7.5±0.6 years. There was not an increased risk of spontaneous and medical abortions for the group of women with seizures during pregnancy compared with those without seizures (Odds ratio [OR]=1.71, 95% confidence interval [CI] 0.18–15.87 and OR=1.26, 95% CI 0.13–12.61,respectively). The rate of preterm delivery was slightly but significantly higher in WWE (8%) compared with controls (2.9%) (OR=2.83, 95% CI 1.03–7.76, p=0.04). Notably, preterm birth was observed in eight women, seven of whom had worsening in seizure control during pregnancy. The risk of cesarean section increased significantly (R=3.39, 95% CI 1.40–8.17, p=0.0066) for women with seizures during pregnancy compared with WWE without seizures.
Conclusion: Seizures in pregnant women with epilepsy are associated with adverse delivery outcomes. Seizure control during pregnancy is an important condition for reducing the risk of complications both for mother and for the child.
Disclosure: Nothing to disclose.

EPO-405

Religious prayers as a manifestation of Temporal Lobe Epilepsy – a case report

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Background and aims: Ictal, interictal and postictal religious phenomenon can be found in epilepsy. Two neuroanatomical structures, the right temporal and frontal lobes, have been identified has critical for processing religion experiences. According to the literature, 0.4% to 3.1% of patients with partial seizures may describe ictal religious experiences, with a clear predominance in patients with temporal focal epileptogenesis.
Methods: The case of a 91-year-old patient in non-convulsive status epilepticus with fluent verbalization of religious jargon is presented.
Results: A previously independent 91-year-old woman was admitted to the Emergency Department confused and with a fluent jargon aphasia, with continuous verbalization of catholic prayers ("Hail Mary"; "Glory be to the father"). On the neurological examination, the patient did not follow simple orders, answer questions, face or follow the examiner. No other neurological deficits were found. Admitting a possible focal status epilepticus, the patient was treated with a levetiracetam perfusion, reversing speech deficits. An electroencephalogram was later performed, revealing focal slowing in the left temporal lobe, without epileptic activity detected. An MRI showed a significant corticosubcortical lesion in the left occipital lobe, with extension to the ipsilateral parietal and temporal lobes, suggestive of a primary central nervous system lymphoma as a possible cause for epileptogenesis.
Conclusion: We describe a rare presentation of temporal lobe epilepsy, characterized by brain imaging and electroencephalographic findings on the left cerebral hemisphere, contrasting to the previously reported cases in the literature, where the right temporal and frontal lobes emerge as the centers for religiosity.
Disclosure: Nothing to disclose.

EPO-406

Sleep-related seizures are associated with poor epilepsy control over preceding year

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Background and aims: Sleep is an important physiological process, playing crucial role in epilepsy. Deprivation from sleep results in higher probability of epileptic seizures. In patients with epilepsy (PWE) primary disorders of sleep could lead to decompensated course of disease. Nocturnal seizures disrupt normal sleep. Our aim was to investigate the effect of sleep-related seizures (SRS) on overall control on epilepsy.
Methods: PWE from tertiary epilepsy and sleep centres were evaluated for seizure frequency during preceding year and were divided into controlled and uncontrolled. We compared those patients with occurrence of seizures in both wakefulness and sleep with PWE whose seizures occurred exclusively during wakefulness. Current antiepileptic drug (AED) use status was taken into consideration. Chi-square test was used for statistical analysis.
Results: The total number of participants was 162, of which males – 85 (52.5%) and females – 77 (47.5%), mean age - 35.5 years (18–71). There were 92 (59.3%) patients who had sleep-related seizures in their clinical pattern, the rest expressing seizures only in wakefulness. The number of uncontrolled patients was 145 (89.5%) versus controlled ones – 17 (10.5%). Chi squared analysis showed a statistically significant association between the presence of seizures from sleep and worse level of seizure control (Chi-Square value - 10.04, $p<0.002$). This link was not influenced by AED use.
Conclusion: Our data suggest that the presence of SRS in PWE could be related to worse yearly control over seizures than in those who do not express seizures from sleep in their clinical spectrum.
Disclosure: Nothing to disclose.

EPO-407

Generalized epilepsy in a patient with GBJ1 X-linked Charcot-Marie-Tooth disease

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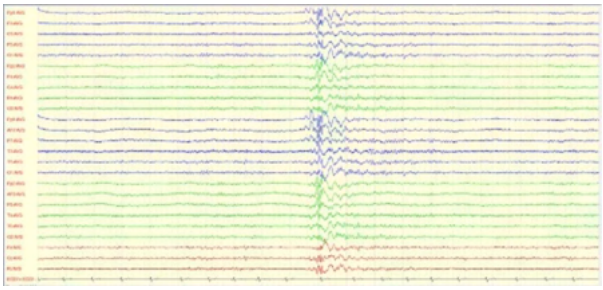
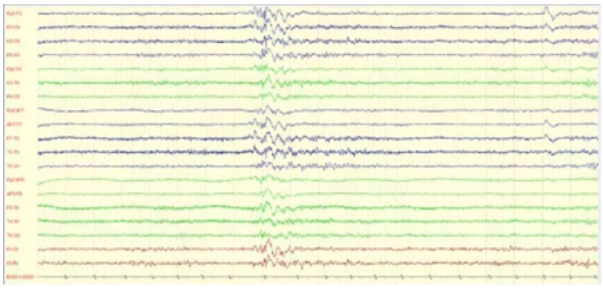
Background and aims: Charcot-Marie-Tooth disease is an inherited neuropathy known for its sensory and motor presentations. The involvement of central nervous system has also been described. In rare cases, epilepsy has been reported however the underlying mechanisms are still not completely understood.

Methods: N/A

Results: We describe a case of a 31-year-old man who was diagnosed with CMT. At the age of eight he started developing gait disturbance with frequent drops. His neurological examination revealed distal weakness and muscular atrophy of the four limbs and his deep tendon reflexes were diminished. His blood tests were unremarkable. An electromyogram disclosed slowing of conduction velocities of both sensory and motor fibers with prolonged distal latencies suggesting a chronic, symmetric axonal sensorimotor polyneuropathy. Genetic test confirmed the diagnose, by showing a pathogenic variant of the GJB1 gene (R183C) consistent with X-Linked Charcot-Marie Tooth. Later, at the age of 21, he developed recurrent unprovoked tonic-clonic seizures. An electroencephalogram performed at this point revealed generalized 3–4Hz polyspike/spike-and-slow-wave complexes, confirming a diagnosis of generalized epilepsy. An MRI excluded structural causes for the patient's seizures. He was then treated with Levetiracetam 500mg twice a day, without recurrence of seizure for a follow-up period of two years.





Conclusion: This report describes a now 31-year-old male with X-Linked Charcot Marie Tooth disease associated with generalized seizures. Genetic studies reported for the first time in our knowledge, a GJB1 mutation in a patient with this unusual association, confirming the diagnosis.

Disclosure: Nothing to disclose.

EPO-408

Validation of the self-assessment cognitive tool “Test Your Memory” (TYM) for people with epilepsy (PWE)

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Background and aims: Cognitive impairment is common in people with epilepsy (PWE). It may significantly affect the quality of life, if not detected and treated early. The TYM test is a short, self-assessment cognitive tool primarily designed to detect cognitive impairment in Alzheimer’s disease. Our aim was to validate the TYM for a cognitive screening of PWE.
Methods: We included 51 PWE and 24 healthy controls. Mean age, education and TYM score were compared between both groups with an independent sample t-test. We draw receiver operator curve (ROC), calculated cut-off value, sensitivity, specificity and likelihood ratio.
Results: PWE had lower mean TYM score than control group (40.90, SD 6.46 vs. 47.83, SD 1.95 points; $p<0.001$), and were younger than control group (47.60, SD 18.14 vs. 62.34, SD 11.86 years; $p<0.001$). There was no differencthe TYM test was 45/46 out of 50 points. Area under the curve was 0,89, sensitivity 72.55 % (CI 58.26 % to 84.11 %), specificity 87.5 % (CI 67.64 % to 97.34 %), likelihood ratio 5.8, and accuracy 77.3 %.
Conclusion: PWE achieved fewer points on TYM than healthy controls, despite younger age. The optimal cut-off is 45/46 points for our population, three points higher than the cut-off for people with Alzheimer’s disease. TYM may be useful as a screening test for cognitive impairment in PWE. However, for more accurate cognitive evaluation, full neuropsychological testing would be necessary.
Disclosure: Nothing to disclose.

EPO-409

Epileptogenic foci evaluation. Comparison between a secondary hospital and a epilepsy unit

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Background and aims: Presurgical evaluation for epilepsy surgery implies a complete battery of imaging, electroencephalographic (EEG) and neuropsychological assessments aimed to find suitable patients. These evaluations usually require high-field MRIs, nuclear medicine imaging, prolonged video-EEG or intracranial EEG recordings to find the epileptogenic zone.
Methods: We present a series of patients derived to a reference neurosurgery service for evaluation, comparing the results of our outpatient studies with the presurgical evaluation results.
Results: We revised a total of 1,475 patients followed since 2009 in our centre. T29 completed the presurgical study and five were suitable and treated. The rest rejected completing the study due to concerns about sequelae. In the evaluation performed in our centre 1.5T MRIs, routine and sleep-deprived EEGs were performed. All patients were diagnosed with focal epilepsy (according to semiology and test results) and were pharmacoresistant. There was a 66,7% of coincidence in the MRI findings, a 50% of coincidence in the EEG findings and an overall 62,5% of coincidence in the suspected epileptic foci. two patients remained seizure free (40%), two had >50% reduction in seizure frequency (50 and 99,5%), and one had a small increase after the procedure. One patient (20%) referred mild cognitive impairment after surgery.
Conclusion: Epilepsy surgery represents an underutilized treatment option for refractory focal epilepsy and should always be considered in pharmacoresistant patients. Patients should be encouraged to consider this option when indicated, with a correct assessment performed in specialized units to obtain the best outcomes.
Disclosure: Nothing to disclose..

EPO-410

Anakinra in the treatment of New-Onset Refractory Status Epilepticus: Our experience from a clinical case

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Background and aims: Recent studies have associated functional and genetic defects in interleukin-1 pathway with New-Onset Refractory Status Epilepticus (NORSE), supporting the use of anakinra in the treatment of this disease; however, the evidence is limited.
Methods: Case-report.
Results: A 23-year-old male, with history of a cousin with epileptic encephalopathy, presented refractory convulsive status epilepticus (SE), preceded by febrile episodes, requiring non-barbituric sedation and admission to intensive care unit (ICU). Blood tests and brain-MRI were normal. CSF analysis showed mild mononuclear pleocytosis, elevated proteins and negative microbiological study. Anti-neuronal and anti-neuropil antibodies in serum/CSF were negative. Initial video-EEG showed diffuse slowing. Full-body CT-scan and testicular ultrasound showed no findings. Nosocomial SARS-CoV-2 infection was diagnosed. Patient presented torpid evolution, persisting fever and seizures, despite anti-seizure drugs and barbituric sedation. Successive video-EEGs showed burst-suppression pattern alternating with multifocal seizures with left frontotemporal predominance, progressing to continuous SE when sedation was reduced. Methylprednisolone, IVIg, plasma exchange and tocilizumab were administered without response. Anakinra 5mg/kg/dose was started with dramatic improvement in level of consciousness and EEG, reverting SE pattern and withdrawing sedation; however, focal and focal to bilateral tonic-clonic seizures persisted daily. Anakinra was removed after four weeks due to neutropenia without aggravation. The frequency/intensity of seizures kept improving until two-per-week. He is currently on third month in ICU and under valproate, brivaracetam, zonisamide, perampanel, ketogenic diet and cannabidiol.
Conclusion: Given the proposed pathophysiology for NORSE, anakinra is an interesting treatment option. We report a positive, although incomplete, response to anakinra. More evidence is required to support this indication.
Disclosure: Nothing to disclose

EPO-411

Immune epilepsy: Clinical characteristics and response to treatment.

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Background and aims: Immune epilepsy (IE) constitutes an increasingly recognized entity. The importance of identifying IE lies in the impact of immunotherapy on its treatment. We aim to analyze the clinical characteristics and response to treatment in patients with IE.
Methods: Retrospective review of patients diagnosed with IE in our center between January/2011–January/2020. A descriptive and comparative analysis of the clinical characteristics and treatment was performed.
Results: 24 patients were included; 14 women (58.3%), with a median age of 36.5 years (IQR: 17-–69). In 58.3% antibodies in serum/cerebrospinal fluid (CSF) were detected, their distribution is shown in Figure 1. 16.7% had paraneoplastic disorders. 62.5% had elevated CSF protein concentration. 58.3% had alterations in brain-MRI, located in the temporal region in 85.7%. All cases presented electroencephalographic alterations: 45.8% presented epileptiform activity, 45.8% focal slowing and 8.4% diffuse slowing. The most common seizure type was focal clonic seizures (45.9%). 41.7% presented status epilepticus, being the cause of death in two patients. The most used anti-seizure drug was levetiracetam (87.5%). 22 cases (91.7%) required immunotherapy, 95.2% with corticosteroids, with clinical improvement in 90.5% and complete remission of seizures in 50%. The improvement of seizures with immunotherapy was more frequent in patients with antibodies detected in serum/CSF (p=0.04). Complete remission of seizure was more frequent in patients with anti-NMDAR antibodies (p=0.04). 46.2% presented cognitive decline and 53.9% focal neurologic deficit.

Figure 1. Distribution of antibodies detected in serum or CSF in patients with IE.

Conclusion: Most patients with IE were treated with immunotherapy with good clinical response and control of seizures. Those with antibodies in serum/CSF, especially anti-NMDAR, presented a better therapeutic response.
Disclosure: Nothing to disclose.

Headache and Pain 3

EPO-412

Headaches and the use of protective personal equipment during the COVID-19 pandemic

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Background and aims: Patients with headache reported worsening of headaches due to personal protective equipment (PPE) use. We aimed to evaluate the association between headache and PPE use during the COVID-19 pandemic.
Methods: A web-based survey was advertised for 12 weeks from September to December 2020, scanning for PPE usage pattern; pre-existing and new-onset headaches after the onset of COVID-19 pandemic and its relation to PPE use.
Results: Of 5064 participants, 90.6%(4562/5034) were women, mean age was 37.2±11 years. 20% of the responders were health-care professionals (993/5046) and 73.7% (3,442/4,476) were working in their workplace when they answered the survey. Surgical and cloth masks were the PPE used most often, protective eyewear was used less frequently, used more often by HCPs, as were FPP2/FPP3 masks. 72% (2,980/4,125) of respondents had previous headaches, 66.9% (1,922/2,873) migraine. About 97% (1,814/1,870) reported aggravation of pre-existing headaches with PPE use. 56% (2,476/4,420) had new-onset headaches. The group of patients with new-onset headaches was more likely to be working at their workplace (2,249/2,476, 90.5% vs 1,635/1,944, 84.2%, $p<0.001$) and wearing PPE for longer time (7±2.7 hours per day vs 6±2.9 hours per day, $p<0.001$). <0.05), with similar frequencies of face mask use (25.4±6.2 vs 25.3±6.4). The multivariate analysis only found mean duration of PPE use to predict patients with a higher risk of new-onset headaches.
Conclusion: Most of the study population developed new-onset headache following PPE usage and/or had an exacerbation of their pre-existing headaches. Duration of PPE usage was the strongest predictor of new-onset headaches.
Disclosure: Nothing to disclose.

EPO-413

Chronic Tension-Type Headache and Serum Vitamin D (25-OH) Levels Correlation

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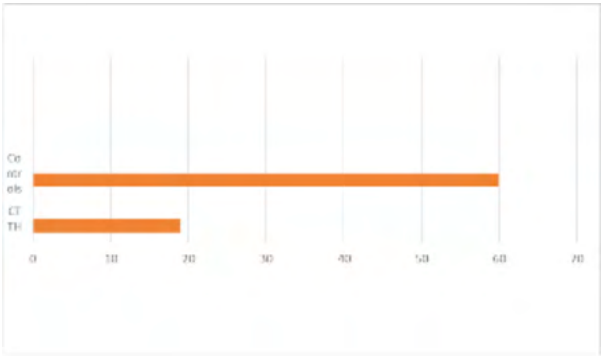
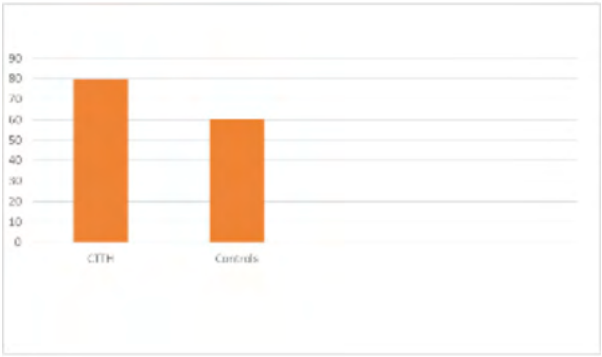
Background and aims: Investigation of studies on chronic tension-type headache (CTTH) made a conclusion of definite communication between CTTH and vitamin D levels. Anecdotal evidence suggests the vitamin D deficiency association with tension type headaches.
Methods: This case-control study was carried out to reveal the association between the chronic tension-type headache (CTTH) and serum vitamin D(25-OH) levels. 100 people 18–50 years old with chronic headache complaints and the same number healthy people were enrolled.
Results: Vitamin D (25-OH) blood levels were lower in patients with headache than in controls (9 and 29ng/ml). Headache patients had high prevalence of musculoskeletal pain (80% vs 60%), muscle tenderness score 4/4 vs 2/4.



Vitamin D blood levels were lower in headache patients



Prevalence of musculoskeletal pain in headache patients

Conclusion: Decreased serum of vitamin D was associated with CTTH, vitamin D supplementation was effective. Further investigation needed to find out if we should call this headache CTTH or secondary headache due to lack of serum vitamin D(25-OH).
Disclosure: Nothing to disclose.

EPO-414

Associated factors of Phantom limb pain: A systematic review and meta-analysis

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Background and aims: Phantom limb pain (PLP) is a highly prevalent and disabling painful sensation following amputation. To date, the exact physio-pathological mechanisms beneath the genesis of PLP remain unclear. We aim to explore potential associated factors in order to increase comprehension of the underlying mechanisms and enhance the development of effective pain preventive and treatment strategies.
Methods: A systematic search in Pubmed/MEDLINE, WOS, Embase and PsycInfo was conducted (until December 25, 2020) following the PRISMA guidelines. We included observational studies assessing the frequency of PLP in amputees that provided data for associated factors. Screening and extraction were done by two independent researchers. We calculated odds ratios (OR) using the raw data (two by two tables), then a random-effects model meta-analysis with logarithm back-conversion were performed to calculate the pooled ORs. Pre/perioperative, epidemiological, and clinical associated factors were evaluated.
Results: We included 31 studies representing 16,360 amputees and 5,982 PLP patients. The assessed factors and pooled estimates are described in Table 1. Female sex, pain prior amputation, general anesthesia, vascular etiology, above knee amputation and comorbidities (phantom limb sensations, residual limb pain, sleep disorders, and depression) were associated with higher odds of PLP. Protective factors were prosthesis use intensity (>8 hours/day) and employment post-amputation.

Factors associated high higher odds of PLP					
Pre/peri-amputation	n	cases	events	OR	CI
Female	13	4782	3291	1.51	1.01 - 2.26
Pain prior amputation	2	676	457	1.51	1.02 - 2.23
General anesthesia	3	7804	463	1.51	1.10 - 2.24
Vascular etiology	5	9919	1770	1.39	1.19 - 1.63
Above knee amputation	6	2243	1241	1.42	1.17 - 1.73
Post-amputation					
PLS	5	1248	774	7.03	2.78 - 17.82
RLP	8	2401	1617	2.46	1.61 - 3.78
Sleep disorders	2	530	170	3.35	2.19 - 5.11
Depression	4	1565	968	2.7	1.87 - 3.9
Associated high lower odds of PLP					
Pre/peri-amputation	n	cases	events	OR	CI
Diabetic etiology	3	7754	467	0.5	0.39 - 0.64
Post-amputation					
Prosthesis >8h/day	4	1329	994	0.56	0.37 - 0.9
Employment	3	503	192	0.42	0.24 - 0.73

n=number of studies, PLS= phantom limb sensations, RLP=residual limb pain

Table 1

Conclusion: We identified a set of factors that underscore the multifactorial etiology of PLP. Besides, we showed potential modifiable factors (anesthesia, prosthesis use, and employment); hence, researchers, clinicians and stake holders could develop interventions to prevent and reduce the appearance of PLP.
Disclosure: No conflict of interests.

EPO-415

Spontaneous intracranial hypotension: epidural blood patch vs conservative management, a case series

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Background and aims: Epidural blood patch (EBP) is an effective treatment for spontaneous intracranial hypotension (SIH). It can be performed either blindly or targeted at the site of the CSF leak. Many centers, however, choose a conservative management based on long rest periods.
Methods: We compared the data of our retrospective series of patients with SIH managed conservatively with a prospective series of consecutive cases in which a targeted EBP was performed.
Results: Five patients were included in the retrospective group (3 men, mean age 40 years) and three in the prospective group (2 men, mean age 36 years). All patients had been documented SIH either by brain MRI, low CSF pressure or both. All cases were studied with CT myelography in order to localize the CSF leak, except one case in which MR myelography was performed. All cases in the retrospective group were managed exclusively with analgesia and rest, having a mean time of recovering of 68.6 days (30–130). None of them had presented any complications of the SIH. The three prospective cases received treatment with an autologous targeted EBP, reporting immediate improvement after the intervention. One case suffered a cortical venous thrombosis as a complication of the SIH, resolved after the EBP. Another patient had a subdural haematoma that required surgery. During the follow-up all patients remained asymptomatic.
Conclusion: In our series, treatment with a targeted EBP was safe, reduced the time of recovery and contributed to the resolution of the complications associated with SIH.
Disclosure: The authors declare no conflicts of interest.

EPO-416

Abstract withdrawn

EPO-417

Galcanezumab in real life: safety and efficacy over 12 months of treatment

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Background and aims: Galcanezumab is a monoclonal antibody targeting calcitonin gene-related peptide. Randomized, placebo-controlled trials demonstrated galcanezumab efficacy in the prevention of Episodic (EM) and Chronic Migraine (CM). However, real life clinical evidence is still poor.

Methods: The present study was conducted at the Headache Centre of Spedali Civili of Brescia. Patients were treated with galcanezumab 120mg monthly, following the 1st 240mg loading dose. Inclusion criteria were: history of migraine for at least 12 months, eight mean migraine days per month (MMD) for at least three months, three previous prohylactic failures. Exclusion criteria were: documented history of cerebrovascular disease and/or myocardiocal infarction, systemic hypertension. Data about outcome, adverse events, analgesics consumption and disability (Migraine Disability Assessment Score Questionnaire – MIDAS; Headache Impact Test – HIT-6) were collected.

Results: 14 consecutive patients were enrolled (3 EM; 11 CM). Baseline clinical and demographic characteristics are shown in Table 1. A significant reduction from baseline to week 4, 12, 24 and 48 in MMD, analgesics consumption and MIDAS score per month was found (Table 2). The percentage of non-responders (<30% MMD reduction), partial-responders (<50%), responders (>50%) and super-responders (>75%) at week 4, 12, 24 and 48 is shown in Figure 1. Side effects were reported in five patients (constipation and injection site local reaction).

	SUBJECTS (n=14)
AGE, years (mean, SD)	46.2 (11.1)
FEMALE, number (%)	14 (100%)
DISEASE DURATION, years (mean, SD)	29.5 (12.7)
PREVIOUS PROPHYLAXIS, number (mean, SD)	5.4 (1.6)
ADD-ON PROPHYLAXIS, number (%)	2 (14.2%)
MEDICATION OVERUSE, number (%)	12 (85.7%)

Table 1: subjects baseline demographic and clinical features.

	BASELINE	WEEK 4	WEEK 12	WEEK 24	WEEK 48	p
MMD Mean (SD)	19.7 (7)	9.9 (8.5)	7.8 (7.9)	5.5 (3.5)	5.3 (2.6)	<0.001
MILD MMD Mean (SD)	9 (6.2)	6.3 (8.4)	5.4 (7.7)	3.3 (2.2)	2.8 (2.7)	=0.01
SEVERE MMD Mean (SD)	10.7 (6.8)	3.5 (3.3)	2.4 (1.6)	2.2 (2.9)	2.5 (1.7)	=0.02
TOTAL ANALGESICS/MONTH Mean (SD)	20.6 (8.6)	10.3 (1.4)	6.8 (5.1)	6.8 (5)	6.6 (5)	<0.001
NSAIDs/MONTH Mean (SD)	9 (10.8)	3.7 (0.9)	3 (4.7)	2.8 (3.2)	1.8 (1.6)	=0.02
TRIPTANS/MONTH Mean (SD)	10.7 (7.6)	6.5 (1.2)	2.3 (1.8)	2.7 (2.9)	4.8 (3.8)	=0.03
MIDAS Mean (SD)	78.9 (75.3)	N/A	15.9 (12.7)	31.2 (25.4)	27.2 (34.2)	=0.01
HIT-6 Mean (SD)	64.7 (4.6)	N/A	53.3 (10)	59 (16.1)	56.4 (7.3)	NS

Table 2: between-subjects ANOVA results documenting a statistically significant reduction in MMD, analgesics consumption, pain intensity and disability.

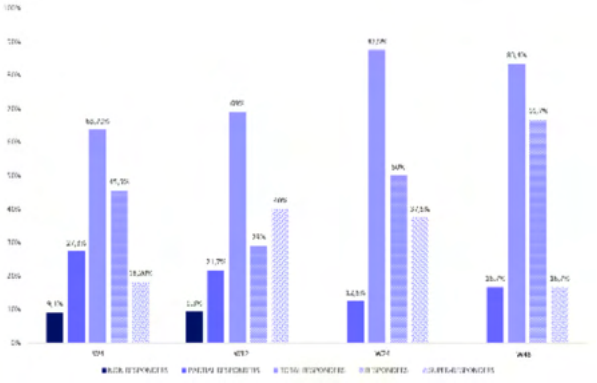

Figure 1: responders rates at week 4, 12, 24 and 48 of treatment.

Conclusion: The data confirm galcanezumab safety and efficacy in migraine prophylaxis. Over 60% of patients documented a significant improvement following the 1st treatment cycle. All patients presented a partial or complete response from week 24.

Disclosure: Nothing to disclose.

EPO-418

The reflex analgesia effectiveness in the complex neuropathic pain treatment

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Background and aims: Study aims to estimate the effectiveness of the classical corporal acupuncture in complex treatment of painful diabetic neuropathy.
Methods: We enrolled 132 patients (81% female and 19% men) aged 18–75 years old with painful diabetic neuropathy that persisted within 0.25–5 years. All the patients were allocated to two groups (66 each) using the sealed envelope method: both groups received gabapentin 900mg/day, study group additionally received a course of 16 sessions of classical corporal acupuncture three times per week every two months. The treatment effectiveness was evaluated by pain intensity measurements with visual analogue scale (VAS) and neuropathic pain scale (DN-4).
Results: The severity of pain prior to treatment was 6,9±1,5 and 7,2±1.3 by VAS, 6,7±2,4 and 7,6±1,9 by the DN-4 in the study and control groups respectively. one month after treatment these figures certainly decreased in the study group comparing with control group both by VAS and by DN-4 – 3,1±1,5 and 5,7±1,9 (p=0,027) and 3,6±1,6 and 5,7±2,5 (p=0,038) respectively. At the end of treatment the severity of pain was 1,3±0,5 by VAS and 2,8±0,9 by DN-4, that was significantly lower than in control group (3,5±1,7; p=0,043 and 4,2±2,1 p=0,046).
Conclusion: The use of the classical corporal acupuncture is effective and safe method in the complex therapy of patients with neuropathic pain.
Disclosure: Nothing to disclose.

EPO-419

Influence of comborbidity on the prevalence of low back pain

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Background and aims: Assessment the effect of comorbidity on the prevalence of low back pain (LBP).
Methods: 3215 people were examined (2470 men). The value of the odds ratio OR=1.0–2.4 was regarded as a weak influence of the factor, at OR=2.5–3.9 the degree of influence is moderate, and at OR>4.0 it is high.
Results: The maximum prevalence of LBP (47.2%) was recorded in the group of 40–49 y.o. In the age category of 50 years and older, the prevalence of LBP decreased to 44.5%. In men who were overweight (BMI>25), the chances of developing LBP increased by 3.09 times, and in women by 4.20 times. In men, the chances of LBP increased 4.72 times in the presence of joint lesions and 7.47 times in neck pain, in women – 2.41 and 5.93 times. The presence of respiratory diseases exerted a moderate degree of influence on LBP development, in men it is 3.02 times, and in women – 2.54 times. Cardiovascular diseases increased OR of LBP by 1.75 times in men, and 2.12 times in women, the pathology of the gastrointestinal tract – 1.78 times in men, 1.15 in women. Smoking increased OR of developing LBP by 1.39 in men and 1.11 in women.

Table 1
Influence of comorbidity on the prevalence of LBP in men

Risk factors	Prevalence of LBP, %	Odds Ratio (95% CI)
Body mass index	59.5	3.09 (1.34-7.11)
Neck pain	77.2	7.47 (5.98-9.32)
Joint diseases	71.6	4.72 (3.77-5.91)
Respiratory diseases	65.3	3.02 (2.32-3.92)
Cardiovascular diseases	51.4	1.75 (1.46-2.09)
Diseases of the gastrointestinal tract	52.5	1.78 (1.46-2.15)
Smoking	44.4	1.39 (1.17-1.64)

Table 2
Influence of comorbidity on the prevalence of LBP in women

Risk factors	Prevalence of LBP, %	Odds Ratio (95% CI)
Body mass index	35.0	4.2 (3.02-9.15)
Neck pain	64.6	5.93 (4.12-8.55)
Joint diseases	52.5	2.41 (1.42-4.08)
Respiratory diseases	54.0	2.54 (1.42-4.52)
Cardiovascular diseases	45.9	2.12 (1.51-2.97)
Diseases of the gastrointestinal tract	35.1	1.15 (0.77-1.62)
Smoking	34.6	1.11 (0.81-1.69)

Conclusion: The study showed a high and moderate degree of influence on the development of LBP: overweight, musculoskeletal disorders and respiratory diseases, and a weak degree of influence of cardiovascular diseases, diseases of the gastrointestinal tract and smoking.
Disclosure: Nothing to disclose.

EPO-420

Efficacy and Safety of Erenumab in Indian Episodic migraine population: India subanalysis of Global EMPOwER study

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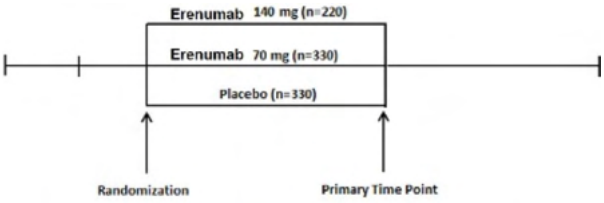
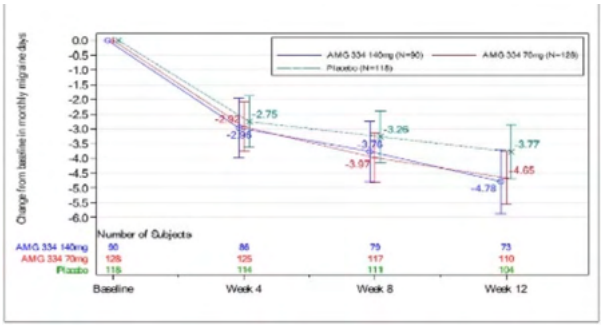
Background and aims: EMPOwER (NCT03333109), a 12-week, double-blind, randomized study evaluated the efficacy and safety of erenumab (70mg and 140mg) in adult episodic migraine patients from Asia, the Middle East and Latin America. This is India sub-analysis of the Global study.

Methods: Indian Patients (n=351) were randomized to receive placebo, erenumab 70mg or 14 mg (3:3:2). Primary endpoint was change from baseline in monthly migraine days (MMD). Secondary endpoints assessed 50% reduction in MMD, changes in headache impact test (HIT-6TM) and safety.

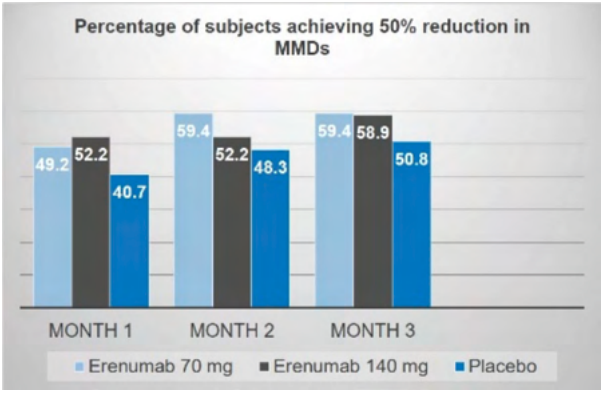


Study Design

Results: At baseline, mean (SD) age was 35.1 (± 8.6) years, 78.9 % were women; mean MMD was 7.82 (2.89). Change in MMD was numerically greater in erenumab groups (erenumab 70 mg and 140 mg) vs placebo (-4.65,-4.78 and -3.77; p vs placebo: 0.174 [70mg] and 0.164 [140mg]). Patients achieving 50% reduction in MMD was higher in erenumab 70mg and 140mg vs placebo (59.4% and 58.9% vs 50.8%; p vs placebo: 0.179 [70mg] and 0.252 [140mg]). Change in HIT-6TM was -7.34 with placebo, -9.65 and -9.40 with erenumab 70mg and 140mg respectively (p vs placebo: 0.032 [70mg] and 0.078 [140mg]). Overall safety profile of erenumab was comparable with placebo with no new safety signals.



Primary Endpoint- Change from baseline in MMDs with Erenumab



Proportion of patients achieving 50% reduction in MMDs

Conclusion: While the study was not powered to evaluate the efficacy of erenumab in the Indian subpopulation, the efficacy and safety profile of erenumab in Indian patients showed improvement numerically for relevant endpoints versus placebo; thus consistent with the global EMPOwER study population.

Disclosure: This was a Novartis sponsored Trial.

EPO-421

Botulinum Toxin Type A Application in The Treatment of Nummular Headache: A Report of two Cases

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Background and aims: Nummular headache (NH) is a relatively rare primary headache disorder with limited treatment options.
Methods: We aimed to share the results of botulinum toxin type A (BoNTA) application in two patients with NH that did not respond to first-line treatments.
Results: Case-1: 32-year old female patient referred with a severe, stabbing headache over a coin-shaped area in the left temporal region. A burning sensation radiating to the face could accompany the headache. Gabapentin (2,400mg/day) was started. While the neuropathic complaints regressed under this treatment, the stabbing headache continued. Therefore, BoNTA was applied subcutaneously to the area where she described the pain. She had a pain-free period for three weeks after the procedure. Two months after, the second dose was administered. She described no change. BoNTA application was deemed ineffective. Case-2: 36-year-old female patient was admitted with a headache over a coin-shaped area in the right parietal region. Gabapentin was started however she could not use it due to the side effects. Therefore, BoNTA was applied subcutaneously to the painful area. There was no change after the 1st application. Two months after, the 2nd dose was administered. Both of the intensity and the frequency of headache were decreased four weeks after the 2nd dose. Now, she is taking BoNTA applications every three months.
Conclusion: BoNTA applications could be evaluated as an alternative treatment for persistent NH in eligible patients with inadequate response to 1st-line treatments.
Disclosure: Authors have no financial disclosure.

EPO-422

Treatment Compliance And Change Of BMI In Long-Term Follow-Up Of Idiopathic Intracranial Hypertension Patients

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Background and aims: Idiopathic intracranial hypertension (IIH) is characterized by headache and visual impairment and frequently seen in women of reproductive age.In this study, it was aimed to evaluate compliance with treatment and changes in body mass index (BMI) of patients with IIH during the follow-up period.
Methods: The files of 106 patients diagnosed with IIH were examined and 41 patients who accepted the phone call were included in the study. Patients who accepted the phone call were questioned about their current symptoms, BMI and treatment compliance.
Results: 41 patients (with a mean age of 35 years were included in the study. The most important risk factor detected in patients was obesity with a rate of 70.7%. The most common symptom was headache (87.8%), followed by blurred vision (53.7%) and temporary vision loss (29.3%). The mean follow-up period of the patients who were evaluated by phone calls was 3.25 years. It was observed that the average BMI of the patients showed a minimal decrease from 32.6 kg/m^2 to 31.2 kg/m^2, and 34.1% of the patients had an increase in BMI during the follow-up period.
Conclusion: IIH can cause permanent visual loss and decrease in visual acuity and requires follow-up due to the risk of recurrence, and it was observed that our patients compliance with treatment was low. In order to have a better prognosis in follow-up, it is important to follow the patients more closely, encourage weight loss, explain the possible risks and consider alternative methods such as bariatric surgery.
Disclosure: To the best of our knowledge, the named authors have no conflict of interest, financial or otherwise.

EPO-423

Off-label use of CGRP monoclonal antibodies in patients with chronic cluster headache

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Background and aims: Monoclonal antibodies (Erenumab and Fremanezumab) that target calcitonin gene-related peptide (CGRP) were recently approved for migraine preventive treatment. These medications were registered in Russia in August 2020, are not yet covered by insurance and are available in pharmacies for patients who have a prescription. We would like to report the results of their off-label use in chronic cluster headache patients.
Methods: Two male patients (30 and 38 years old) with chronic cluster headache, both using 960mg of Verapamil with mild effect, were consulted in a headache clinic. The first patient had 2-3 attacks per day lasting 40–120 minutes, the second – 1–3 attacks per day lasting 30–180 minutes. Attack management with oxygen and sumatriptan was insufficient. The patients were prescribed monthly injections of Erenumab 140mg and Fremanezumab 225mg, respectively, considering their efficacy, safety and expected trials in cluster headache patients (medication choice was based on the patients' economic preferences).
Results: The 1st patient had three injections to this point; he notes a reduction in the number and intensity of the attacks (0–1 attack per day), which are now managed using an external trigeminal nerve stimulation device for 20 minutes. Currently, the patient has pain-free episodes that last up to 10 days. The second patient had four injections and reports 0-1 attack per day, lasting no more than 60 minutes, which can be aborted by oral sumatriptan.
Conclusion: CGRP monoclonal antibodies may be effective in patients with chronic cluster headache. However, clinical trials are needed to prove efficacy on a large group of patients.
Disclosure: Nothing to disclose.

EPO-424

Cluster-tic syndrome associated with trigeminal vascular crossing

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Background and aims: Cluster-tic syndrome (CTS) is a recognized entity in ICHD-III, it consists on the coexistence of cluster headache attacks (CR) and trigeminal neuralgia (TN) in the same patient. We present a case of SCT associated with trigeminal vascular crossover (TVC).
Methods: 73-year-old male patient, who consulted for episodes of strictly unilateral right headache, described as attacks of right periocular pain, lacinating or burning, associating conjunctival injection, eyelid edema, miosis, lacrimation and ipsilateral rhinorrhea with spontaneous resolution in about two hours and frequency of 9–10 attacks per day. It associates psychomotor restlessness and cutaneous allodynia in the malar region and trigger points, triggering pain when shaving or chewing.
Results: Physical examination shows eyelid edema, lacrimation, conjunctival injection, and right miosis. Neurological examination resulted normal. Brain and cranial base MRI was performed with SSFP sequence in which a right CVT with vertebral artery was observed. During admission, the headache is refractory to treatment with verapamil, CBZ, TPM, LCS and BA of right NOM. Finally, he presented clear improvement when starting VPA perfusion and subsequent maintenance treatment with three VPA 500 mg tablets per day, remaining pain free.
Conclusion: The diagnosis of CTS is very rare, being limited to few reports in the literature. Patients with this entity should be assigned both the diagnosis of CR and TN, since both disorders have to be treated in order to free the patient from pain.
Disclosure: Nothing to disclose.

EPO-425

The influence of cgrp on sensitization in posterior cerebral artery territory in migraine

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Background and aims: The sensitization with neurogenic inflammation in the territory of posterior cerebral artery (PCA) seems to be important issue in migraine headache and aura. The vasodilatation of PCA is probably important component of trigeminovascular sensitization and could be detected by transcranial Doppler (TCD). Exogenic CGRP might augment the sensitization. Therefore, we studied the hemodynamic and clinical responses to CGRP in PCA using TCD.

Methods: 20 healthy subjects and patients with migraine participated our study. TCD was used to monitored mean arterial velocity in posterior cerebral artery (vm PCA). Intravenous infusion of CGRP 1.5mcg/min was given and a 10 min period after the application of CGRP. We monitored CGRP induced headache. The statistical analysis of the parameters was done using ANOVA and logistic regression.

Results: We found significant decrease of vm PCA during CGRP infusion and after it in both groups ($p<0.005$), Et.CO2 changes were significant predominantly in migraine ($p<0.005$). ANOVA did not show significant increase in vm PCA responses ($p>0.05$), but vmPCA responses were associated with migraine ($p=0.025$) Et-CO2 responses were significantly higher in migraine during CGRP infusion ($p<0.020$). HR response did not differ significantly between the groups ($p>0.30$), while MAP response were significantly differ between the groups ($p<0.05$) during CGRP infusion. CGRP headache is associated with vm PCA ($p=0.003$).

Conclusion: In conclusion, our data indicate that CGRP induces PCA vasodilatation and CGRP induced headache in migraineours. The sensitization in PCA territory is important component of migraine episode.

Disclosure: Nothing to disclose.

Infectious diseases 2

EPO-426

Herpes Encephalitits, the role of Decompressive Craniectomy: a case report and literature review

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Background and aims: Herpes simplex encephalitis (HSE) is a viral infection of the central nervous system that carries a high morbidity and mortality rate. In severe cases, the evidence supporting the surgical management of HSE associated with refractory brain oedema is of low quality. Most papers reported in the literature are case reports of interventions that include decompressive craniectomy (DC) and temporal lobectomy.
Methods: Case report
Results: A 30-year-old woman with severe HSE that rapidly progressed to a comatose state with status epilepticus. Due to the rapid development of brain oedema with midline shift and uncal herniation, it was decided to perform a right fronto-parieto-temporal DC. She had a slow but favourable postsurgical recovery, maintaining apathy, disartria and mild cognitive impairment. She was discharged after a long hospital stay of 65 days to a rehabilitation centre, mainly focusing in neurocognitive and speech therapy.
Conclusion: DC in herpes simplex encephalitis is rarely performed and lacks strong scientific evidence. However, it seems that in refractory intracranial hypertension, compression of the basal cisterns and/or midline shift, the DC is not only lifesaving but also improves the outcome despite the underlying pathology. A detailed literature review of DC in this disease is also presented.
Disclosure: No disclosures.

EPO-427

Strokes in patients with HIV infection

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Background and aims: The risk of stroke in patients under 45 years with AIDS is 10 times higher than in the same age population in general. The main purpose is to study the features of the course of stroke in patients with HIV infection.
Methods: We examined 73 patients with stroke hospitalized in the vascular centers of St. Petersburg. Group 1 is HIV-positive (33 patients, mean age 49±11 years); group 2 is HIV-negative (40 patients, 49±7 years). Depending on HIV and the type of a stroke – hemorrhagic (HS) or ischemic (IS) groups were divided into 1a (n=8, HS) and 1b (n = 24, IS), 2a (n=12, HS) and 2b (n=28, IS).
Results: At the stage A1 of HIV infection stroke was observed more often (45.5%) than on the other stages. HIV-positive patients had low viral load (55%), opportunistic infections (21.3%), rarely was cardioembolic stroke. HS stroke in the 1st group was characterized by a meningeal syndrome and thrombocytopenia, IS – headache syndrome, lymphopenia, thrombocytopenia, increased ESR, ALT and AST enzymes. HIV-positive patients showed insignificant regression of neurological symptoms (2 points, NIHSS) compared with HIV-negative (4 points). Risk factors of CeVD were not identified in 12.5% of patients with HIV and IS, vasculopathy was assumed in 62.5% of patients with HS.

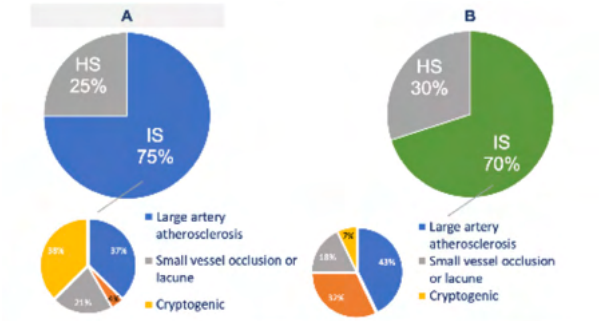

Fig. 1. Types of stroke in patients with HIV-infection (*A*) and without HIV-infection (*B*)

Types of stroke in patients with HIV-infection and without HIV-infection

Table 1. The main clinical and laboratory parameters in examined patients

Parameters	1a (n=8)	2a (n=12)	p (1a-2a)	1b (n=24)	2b (n=28)	p (1b-2b)
Neurological deficit	100% (8)	100% (12)	>0,05	100% (24)	100% (28)	>0,05
Meningeal symptoms	62,5% (5)	8,3% (1)	<0,05	4,2% (1)	0% (0)	>0,05
Paroxysmal syndrome	50% (4)	16,7% (2)	>0,05	12,5% (1)	10,7% (3)	>0,05
Headache	37,5% (3)	16,7% (2)	>0,05	29,2% (7)	7,1% (2)	<0,05
Leukocytosis	12,5% (1)	50% (6)	>0,05	16,7% (4)	21,4% (6)	>0,05
Lymphopenia	25% (2)	25% (3)	>0,05	37,5% (9)	10,7% (3)	<0,05
Increased ESR	62,5% (5)	50% (6)	>0,05	58,3% (14)	21,4% (6)	<0,05
Lymphopenia and increased ESR	25% (2)	25% (1)	>0,05	25% (6)	3,6% (1)	<0,05
Thrombocytopenia	75% (6)	16,7% (2)	<0,05	29,2% (7)	3,6% (1)	<0,05
Increased ATL and AST	75% (6)	33,3% (4)	>0,05	33,3% (8)	3,6% (1)	<0,05
Increased fibrinogen	25% (2)	41,7% (5)	>0,05	33,3% (8)	17,9% (5)	>0,05

Fn. 1a — patients with HIV-infection and HS, 2a — patients with HS, 1b — patients with HIV-infection and IS, 2b— patients with IS, p — significance test for comparison between indicators.

The main clinical and laboratory parameters in examined patients

Table 2. Comparative analysis of clinical and neurological indicators in patients of group 1 and group 2

	Group 1 (n=33)		Group 2 (n=40)		p
	before treatment	after treatment	before treatment	after treatment	
NIHSS in points	7 (4;11,1)	4 (2;8,5)	8,5 (4;12)	3 (1;5,7)	
Regress NIHSS in points	2 (0,1;4)		4 (2;7,8)		<0,05
Time of hospitalization from the onset of the disease	17 (4,25;48)		4,25 (2,18)		<0,05
Patient-bed-days	10 (4,8;15)		15 (12;24)		>0,05

Fn. 1 group — patients with HIV-infection and stroke, 2 group — patients without HIV-infection with stroke.

Comparative analysis of clinical and neurological indicators in patients of group 1 and group 2

Conclusion: HIV increases the risk of stroke more often on asymptomatic stage. Insignificant regression of symptoms and hard course of disease are caused by opportunistic diseases, coinfections, hemostasiological disorders and the absence of HAART.
Disclosure: Nothing to disclose.

EPO-428

Epidemiological burden of meningitis in a city of southern Brazil: an analysis from 2010 to 2019

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Background and aims: Meningitis can be defined as an inflammation of the arachnoid membrane, the pia mater and cerebrospinal fluid. The effects of meningitis on public health can change in accordance with a etiologic agent, lethality and production capacity of disease outbreak. The aim of this study was to describe the number of reported cases of viral and bacterial meningitis, as well as the lethality rates from 2010 to 2019 in a city in Southern Brazil.
Methods: An ecological study was carried out in January 2021 from the health information of the Brazilian Health Unified System databases. The analysis comprised the number of meningitis cases notified from 2010 to 2019 in Passo Fundo, a Brazilian southern city. The mortality rate also was analyzed. To calculate the lethality rate, the number of deaths by cause was used as the numerator, and the number of notified cases of the disease as the denominator. Descriptive statistics were performed though absolute (n) and relative (%) frequencies.
Results: The highest incidence rate (66.5 cases per 100.000 inhabitants) was observed in 2015, with a lethality rate of 4%, On the other hand, the lower incidence was identified in 2019 (34 cases per 100.000 inhabitants) with a lethality rate of 3.1%. In 2013 there was the highest lethality rate among the years analyzed (13.5%) while 2011 had the lowest rate (0.9%).
Conclusion: Knowing the epidemiology burden of meningitis allow to develop targeted actions for the treatment and prevention.
Disclosure: No disclosures.

EPO-429

Meningoenchephalitis secondary to epstein-barr virus reactivation with cerebrospinal fluid glucose consumption

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Background and aims: Epstein-Barr Virus (EBV) meningoencephalitis mostly occurs in young patients as a consequence of Central Nervous System (CNS) spread after primary infection.
Methods: We present a clinical case of an immunocompetent patient admitted to the hospital, with meningoencephalitis secondary to a reactivation of EBV in CNS with cerebrospinal fluid (CSF) glucose consumption.
Results: A 75-year-old woman without medical records, presented with a three days history of fever, altered mental status and gait instability. The neurological exam revealed disorientation, decrease level of consciousness, confusion and meningism. Complementary studies including laboratory tests, neuroimaging techniques and electroencephalogram (EEG) showed no relevant findings, but the lumbar puncture disclosed mild lymphocytic pleocytosis, elevation of protein's level and glucose consumption, findings suggestive of Mycobacterium Tuberculosis or Listeria's infection. However, the microbiological and nucleic acid based tests unveiled significant presence of EBV-DNA in CSF and serum IgG antibodies, with moderate EBV load (2x10^3 DNA copies/ml). Consequently, treatment with intravenous Aciclovir was started. Asymptomatic the patient was discharged within three weeks. One month later, the patient presented a self-limited episode of speech arrest and altered mental status. The EEG and perfusion MRI showed pathologic findings in the left hemisphere (figure 1) that were compatible with epileptic discharges probably secondary to CNS changes after EBV infection.

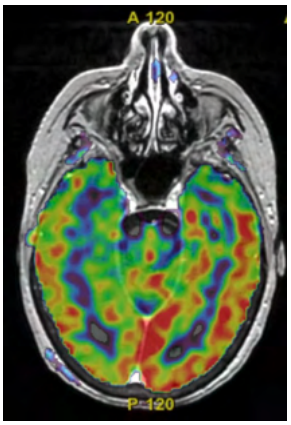

figure 1. Perfusion MRI shows an increased cerebral blood flow (CBF) in the temporo-occipital left lobe

Conclusion: EBV reactivation might cause a meningoencephalitis with CSF glucose consumption in an immunocompetent patient. Therefore, this CSF results should not rule out a viral infection, if suspected. However, further investigations are needed for a better understanding of this entity.
Disclosure: The Authors declares that there is no conflict of interest.

EPO-430

Borrelia Infection and Tumor-like Demyelinating Lesion Delaying the Diagnosis of Multiple Sclerosis: A Case Report

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Background and aims: The diagnosis of multiple sclerosis (MS) may be difficult in some instances due to a great number of conditions that should be excluded. Lyme neuroborreliosis may manifest with episodic focal neurological deficits which makes the diagnosis of MS even more difficult. The aim of our study is to present the case of a patient with MS where the presence of Borrelia infection and a tumor-like cerebral lesion made the diagnosis a challenge.
Methods: We present the case of a 27-year-old female who presented two episodes of focal neurologic deficits which remitted to corticotherapy one year prior to admission. She preformed serial cerebral MRI which revealed multiple T2WI/FLAIR hyperintensities and hypointensities on T1WI, many with gadolinium enhancement, one of the lesions having a tumor-like appearance. The serum IgM antibodies for Borrelia (IgMAB) and Toxoplasma were positive and the patient received ceftriaxone and albendazole and referred for cerebral biopsy.
Results: She was admitted to our clinic for another relapse. Beside cerebral MRI, we performed cervical-thoracal MRI which revealed two lesions, visual evoked potentials with prolonged p100 latencies and IgMAB (western-blot) from cerebrospinal fluid (BA-CSF). The histopathological exam confirmed the presence of demyelinating lesions. Two months later the patient had another relapse, BA-CSF being negative. MS treatment was initiated with only one relapse in the next three years.
Conclusion: We chose to present this case to underline that sometimes the diagnosis of MS can be confounded due to the co-occurrence of other diseases which can delay it, leading to accumulation of lesions and disability.
Disclosure: Nothing to disclose.

EPO-431

Listeria rhomboencephalitis – a diagnostic conumdrum

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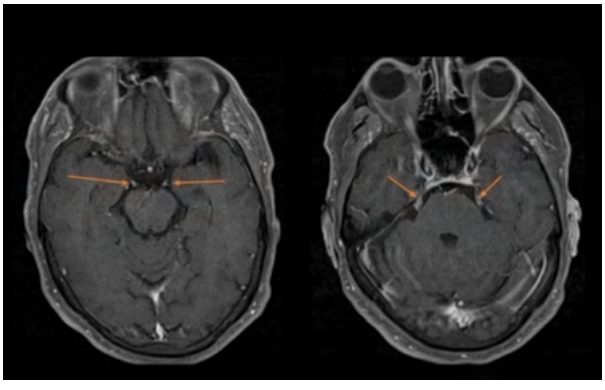
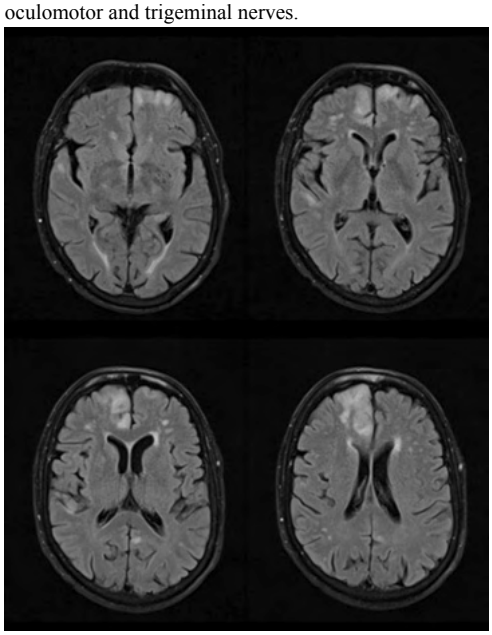
Background and aims: Listeria monocytogenes has a notorious tropism for the CNS. Listeria rhomboencephalitis has a typical biphasic presentation with fever and headaches preceding brainstem and cerebellar signs.
Methods: We report the case of a Listeria rhomboencephalitis with atypical features.
Results: A 62-year-old man with no previous medical history presented to our emergency department with progressive gait difficulties over the past three weeks. There was no history of fever or other symptoms. Neurological examination revealed left ptosis, complex ophtalmoparesis, bilateral dysmetria and broad-based gait. Over the past days he developed nearly complete ophtalmoparesis, areflexia and marked gait ataxia. Brain MRI was reported as normal, but in retrospect showed subtle abnormalities. Lumbar puncture revealed 44 leukocytes/mm^3 (91% mononuclear) and elevated proteins. Gram stains and CSF cultures were negative. Intravenous immunoglobulins were administered under the hypothesis that it was a Miller Fisher syndrome. The patient continued to worsen, developing seizures, hemiparesis and respiratory failure. He was transferred to an ICU and started treatment with ceftriaxone and ampicillin. The patient slowly recovered but developed toxicoderma and antibiotics were ceased. A new MRI revealed areas of corticosubcortical edema with cortical cytotoxic restriction. CSF Lysteria monocytogenes PCR came back positive, so he was treated with trimethoprim-sulfamethoxazole for four weeks. He continued to improve and was discharged walking autonomously. Repeat MRI at one month showed near complete resolution of the signal abnormalities.

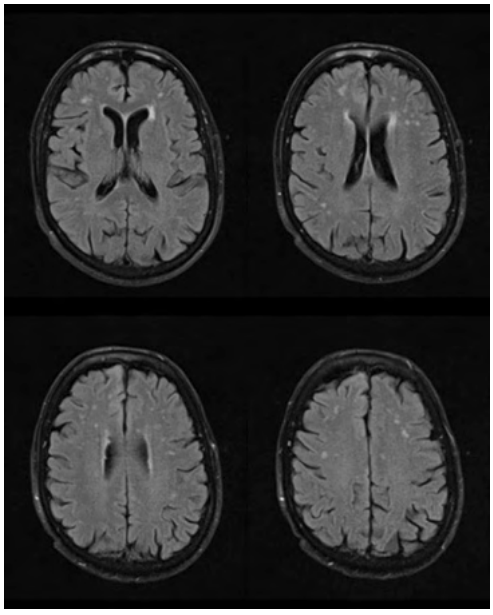


Postcontrast axial T1WSE shows bilateral enhancement of the

oculomotor and trigeminal nerves.



Axial T2W-FLAIR performed 20 days after the first scan shows hyperintensities in the right frontal parasagittal and left frontobasal regions. These areas also revealed cortical diffusion restriction (not shown).



Axial T2W-FLAIR follow-up performed one month after shows near complete resolution of the T2 hyperintensities, persisting subtle T2 hyperintensity in the right frontal parasagittal area.

Conclusion: This case illustrates a Listeria rhomboencephalitis with a protracted course in the absence of fever or immunosuppression. It also supports the use of trimethoprim-sulfamethoxazole in patients with penicillin hypersensitivity.
Disclosure: No disclosures.

EPO-432

Neurologic complications of fungic endocarditis

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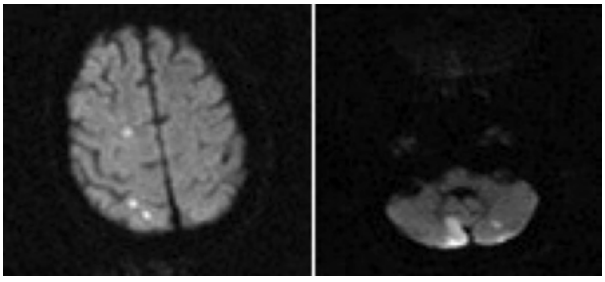
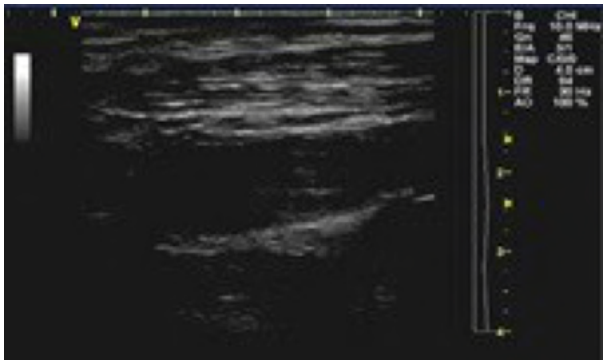
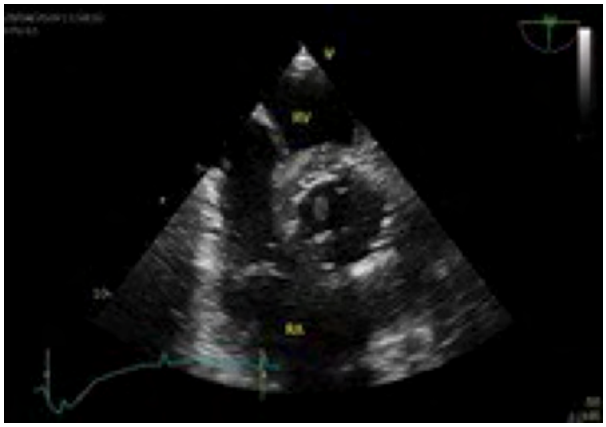
Background and aims: An infectious endocarditis can cause ischemic stroke due to septic embolization, with clinical manifestations in 10–35% of patients.
Results: 70 year-old man with hypertension and diabetes mellitus, previously submitted to aortic valve replacement for severe stenosis and endarterectomy of the right internal carotid artery (ICA). Admitted to the ER due to sudden onset of imbalance with right cerebellar ischemic stroke on CT. Brain-MRI showed additional recent ischemic lesions in the anterior and posterior vascular territories, bilaterally. Cervical doppler revealed a pediculated hypoechogenic mobile thrombus in the right bulb/ICA transition, with subocclusive flow. Blood cultures revealed Candida parapsilosis, and he was started on micafungin. Transesophageal echocardiogram identified a mobile vegetation in the aortic valve suggesting fungal endocarditis with active embolic foci. He underwent a new aortic valve replacement. During hospitalization, he presented an acuted confusional syndrome and persistent fever. CSF disclosed mononuclear pleocytosis, proteinorrachia and OCB, without isolation of microorganisms. Repeated brain-MRI identified brain abscess in the frontal region, initiating treatment with amphotericin and flucytosine. Serial dopplers were performed, and on the 45th day of treatment with antifungal agents resolution of the mobile vegetation was documented. The patient presented progressive improvement with mild paraparesis and left appendicular dysmetria. Due to clinical stability and imaging resolution of the lesions he was discharged under oral antifungal treatment.



Recent ischemic lesions in the anterior and posterior vascular territories bilaterally



Pediculated hypoechogenic mobile thrombus in the right bulb/ICA transition, with subocclusive flow



Mobile vegetation (17mm) in the aortic valve

Conclusion: Fungal endocarditis can cause stroke, brain abscess and encephalitis/meningitis. There is no data on the frequency of concomitant vegetation in ICA in cases of IE, but early cerebrovascular Doppler can help with timely diagnosis and therapeutic decision.
Disclosure: Nothing to disclose.

EPO-433

Human immunodeficiency virus (HIV) seroconversion presenting with Guillain-Barré Syndrome (GBS): a case report

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Background and aims: GBS is a heterogeneous condition which usually presents as an acute, monophasic paralyzing illness provoked by a preceding infection. HIV can cause a range of neurological disorders including GBS. GBS can occur at any stage of HIV infection, but usually at seroconversion. A 31-year-old male presented with lumbar back pain radiating to both legs, and asymmetric muscle weakness of the upper and lower extremities. He reported no previous medical history. On the second day of his admission, patient developed right facial nerve palsy. His neurological examination revealed reduced strength in the upper and lower limbs, areflexia and sensory loss in a glove and stocking distribution.
Methods: Lumbar puncture revealed lymphocytic pleocytosis (WBC count 90/L) and elevated protein values of the CSF (300 mg/dl). EMG findings were consistent with demyelinating sensorimotor polyneuropathy. CSF multiplex PCR, and CSF and serum studies for HSV, EBV, VZV, Toxoplasma gondii, Lyme disease, Rickettsia, West Nyle virus, Cryptococcus neoformans, Coxiella burnetii, syphilis were negative.
Results: HIV antibody testing was positive, while his viral load 125.000/ml, and CD4 count 565/mm3 indicated a recent infection. Treatment with IVIG was started immediately on his first day of admission, while highly active antiretroviral therapy (HAART) was initiated after confirmation of HIV infection. Patient's symptoms gradually improved and one month after discharge his neurological examination was normal.
Conclusion: GBS can be, in rare cases, the first manifestation of HIV infection. Simultaneous treatment with IVIG and HAART accelerates therapeutic outcome. An HIV test in every individual with GBS is recommended.
Disclosure: Nothing to disclose.

EPO-434

Neurocysticercosis presenting with a single nodular lesion – a diagnostic challenge

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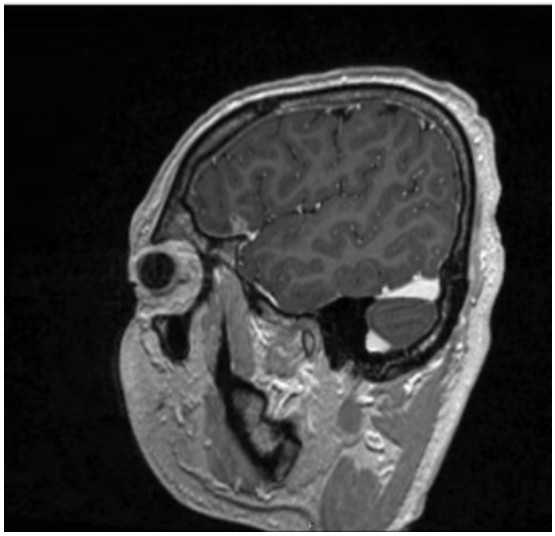
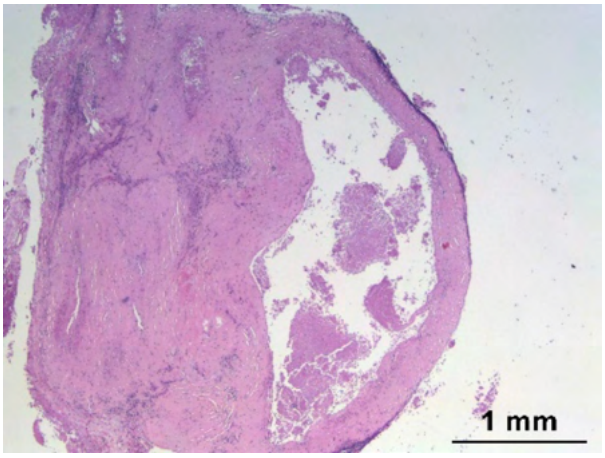
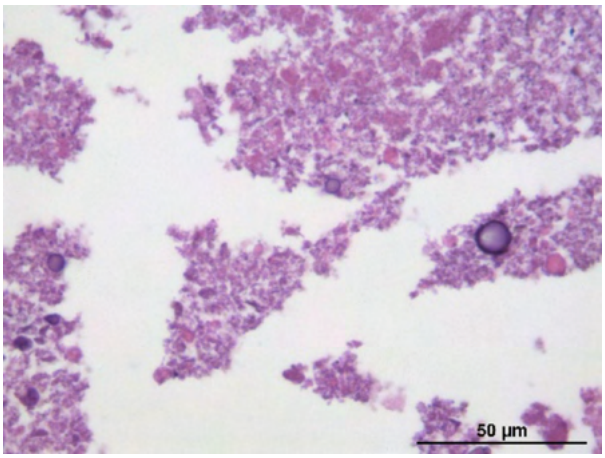
Background and aims: Parasitic infections of the Central Nervous System are an important cause of morbimortality worldwide, especially in developing countries.
Methods: Case report.
Results: We present a 24-year-old Nepalese male, living in Portugal for the past six months, with no relevant past medical history. He was admitted to the Emergency Room with convulsive status epilepticus and a sepsis secondary to pneumonia, with hypoxemia requiring sedation and invasive mechanical ventilation for three days. He was seizure free after four days of anti-epileptic treatment. Neurological examination was unremarkable. Brain MRI revealed a right frontal subcortical lesion with T2 hyperintensity raising the hypothesis of a low-grade glioma. Blood panel showed leukocytosis with neutrophilia and increased C-reactive protein and CSF analysis showed mild hyperproteinorrachia. Anti-Taenia solium antibodies were negative in the serum and CSF. HIV, anti-toxoplasma antibodies and CSF cultures for Mycobacterium tuberculosis were negative. A brain biopsy was performed and confirmed the presence of an encapsulated, intraparenchymal necrotic lesion with cellular debris and rounded calcified structures, suggestive of neurocysticercosis. The patient was started on praziquantel, albendazol and dexamethasone. After six months of follow-up, he remains clinically stable and without new lesions in the MRI.





Brain biopsy



Brain biopsy2

Conclusion: Neurocysticercosis (infection with Taenia solium) is the one of the most common parasitic infection of the CNS and its diagnosis can be challenging, especially when it presents with a single nodular lesion mimicking a cerebral tumor. With increasing globalization and integration of patients from all over the world, parasitic infections must be considered in the differential diagnosis of these cases.
Disclosure: Nothing to disclose.

EPO-435

Subdural empyema mimicking ischaemic stroke

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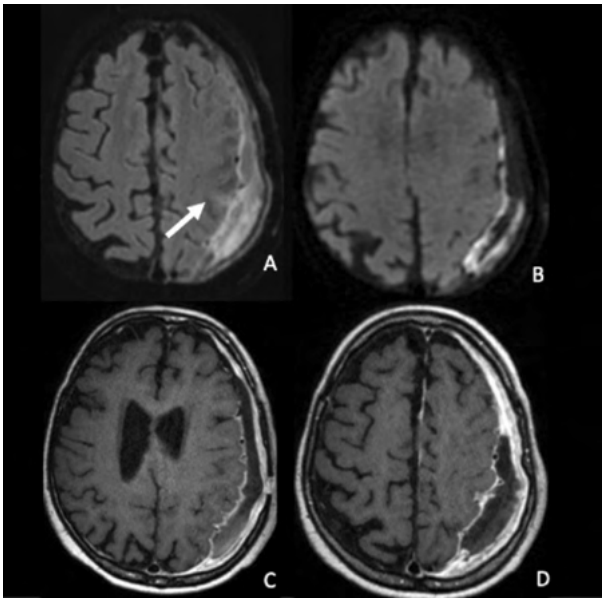
Background and aims: Subdural empyema is a rare intracranial infection, commonly seen as a complication of neurosurgical intervention, skull trauma, sinusitis and otitis media. Treatment requires surgical evacuation of the collection and administration of appropriate antibiotics.
Methods: n/d.
Results: A 78-year-old male with multiple vascular risk factors and history of surgical drainage of a left parietal post traumatic subdural hematoma two months before, without neurological sequelae, was admitted with difficulty articulating words and worsening vision. Neurological examination revealed dysarthria and right homonymous hemianopia. There was no evidence of acute parenchymal changes on CT, persisting a left subdural collection. A diagnosis of ischaemic stroke was admitted. During admission, he developed an acute confusional state, fever and discrete elevation of inflammatory parameters. An MRI was performed with no evidence of acute ischaemia. On DWI there was evidence of areas of increased signal in the interior of the collection and had contrast enhancement after administration of gadolinium. There was also evidence of adjacent parenchymatous lesions, suggestive of subdural empyema with associated cerebritis. Emergent surgical evacuation was performed, and he was treated with vancomycin and meropenem. Microbiological analysis revealed isolation of Staphilococcus capitis. The patient was discharged with no focal deficits.



A – axial T2 FLAIR; B – axial DWI; C and D – axial T1 after gadolinium. Left frontoparietal subdural collection with restricted diffusion. Evidence of contrast enhancement and some areas with parenchyma involvement (cerebritis - white arrow).

Conclusion: Subdural empyema is a condition that is associated with significant morbidity and mortality and requires early diagnosis and prompt treatment to improve patient outcome. Our case highlights the importance of being aware to this condition, especially in patients with predisposing factors.
Disclosure: Nothing to disclose.

EPO-436

Encephalitis - the clinical spectrum of a tertiary hospital

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Background and aims: Encephalitis is an acute inflammation of the brain parenchyma, caused by infectious conditions, predominantly from viral etiology or autoimmune. However, in about half of the cases, the etiology remains undetermined.
Methods: Retrospective analysis of consecutive cases of patients with encephalitis admitted between 2010-2019 at Hospital Egas Moniz. Patients were divided into three subgroups: infectious, viral encephalitis without an identified agent, and immune-mediated.
Results: A total sample of 42 patients, with an average age of 59.81±16.2 years, 52.4% of the male gender. 26.2% of encephalitis with isolated infectious agent were identified, being the most common etiology herpetic encephalitis (54.6%, n=6); 45.2% viral encephalitis without an agent and 28.6% immuno-mediated encephalitis. The most common clinical manifestations identified were changes in behavior (43%, n=18), epileptic seizures (38%, n=16) and language dysfunction (33%, n=14), with an average duration of the symptoms of two days. The EEG showed changes in 61.9%, the majority diffuse slowing of the tracing (33% n=12), and the MRI in 47.6% (n=20). 42.9% (n=18) had side effects, the majority due to memory impairment, and the mortality rate was 7.1% (n=3).
Conclusion: In our cohort, most patients were diagnosed with viral encephalitis without an identified agent (45.2%). The mortality rate was 7.1% and the percentage of side effects in the follow-up period was substantial (42.9%), with memory impairment being the most common dysfunction.
Disclosure: Nothing to disclose.

Movement disorders 2

EPO-437

Non-dopaminergic freezing

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Background and aims: Freezing of gait (FOG) is a common neurological manifestation in parkinsonian syndromes and it's defined as the inability to generate effective stepping movement. Its pathophysiology is poorly understood.
Methods: Here we report three cases of typical FOG in the context of unremarkable brain MRI and dopaminergic presynaptic imaging.
Results: Patient1 (65-year-old) had developed gait difficulties in few months, with short stepped-gait and start-hesitation. The neurological examination revealed clear pyramidal signs and a severe tremulous cervical dystonia. A typical FOG was present. Cervical MRI showed cervical compression myelopathy. Patient2 (64-year-old) is a man with SPG7. He described recent difficulties in initiating gait and turning. On examination, he had typical FOG, more evident during turning or starting. Patient3 (56-year-old) described generalized stiffness and muscle cramps, followed by gait initiation impairment. On examination she had brisk reflexes, prominent lordosis, lower limb stiffness and FOG. A diagnosis of stiff person syndrome was made.
Conclusion: FOG pathophysiology is poorly understood, but a direct correlation with the dopaminergic state of patients is not clinically evident. Recently, imaging studies in freezers have demonstrated white matter alterations and consequent network disruption between cortical, subcortical and brainstem areas. Indeed, gait is now considered a higher function, integrating motor abilities and cognition, with involvement of cortical and subcortical hubs. FOG could therefore be an expression of network disruption, with basal ganglia being one but not the only hub involved. Taken together, our exemplary cases show that FOG can occurs in patients with intact presynaptic dopaminergic neurons, supporting the hypothesis of the involvement of other non-dopaminergic networks.
Disclosure: GDL was awarded with the EAN research fellowship 2020.

EPO-438

Abstract withdrawn

EPO-439

Efficacy of opicapone according to different levodopa daily frequencies in Parkinson's patients with motor fluctuations

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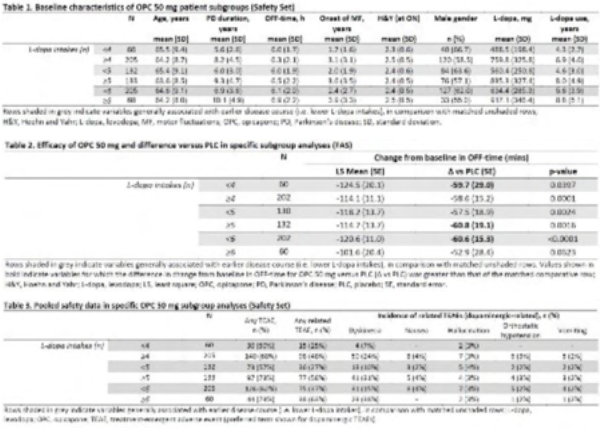
Background and aims: Opicapone (OPC) proved to be effective in treating end-of-dose motor fluctuations (MF) in Parkinson's Disease (PD) patients [1,2].
Methods: Matching OPC 50mg and placebo (PLC) data from BIPARK-I and II [1, 2] were combined. The studies had similar designs, eligibility criteria and methodologies. Primary efficacy endpoint was change from baseline in absolute OFF-time. Safety was assessed by evaluating the incidence of treatment-emergent adverse events (TEAEs). Subgroup analyses were performed to evaluate consistency and potential trends between subgroups based on different levodopa daily intakes at baseline (Table 1). Efficacy pairwise subgroup analyses were performed using Analysis of Covariance. Safety assessments were analysed descriptively.
Results: Overall, 522 patients were randomised to PLC (n=257) and OPC 50mg (n=265) (Table 1). OPC 50 mg was significantly more effective than PLC for all subgroup analyses ($p<0.05$), except for the subgroup of patients treated with six levodopa daily intakes (p=0.0623; Table 2). Moreover, OPC 50 mg demonstrated enhanced magnitude of effect in patients who had less frequent levodopa intakes (Table 2). There was also a trend towards a lower incidence of dopaminergic-related TEAEs in the same subgroups of patients (Table 3).



Conclusion: These findings indicate that OPC 50mg is efficacious in the full spectrum of motor fluctuations and there is no reason to delay its introduction.
Disclosure: 1.Ferreira et al., Lancet Neurol. 2016;15(2):154-165; 2.Lees et al., JAMA Neurol. 2017;74(2):197-206.

EPO-440

Floating Door Sign - graphomotor functions assessment in patients with Parkinson's Disease and Essential Tremor

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Background and aims: The ability to replicate figures requires preservation of visuospatial functions and motor pathways. The "floating door sign" (FDS) reflects the inability to join the vertical lines of a door with the floor (1mm) when a patient is asked to draw a house. This signal was described as a positive predictive factor for Parkinson's Disease (PD) but not for Essential Tremor (ET). We aimed to evaluate the features of the FDS and other graphomotor tasks in patients with PD and ET.
Methods: We asked patients from two hospital centres to copy three drawings (house, flower and sun), write a sentence and perform two cognitive tests (pentagons copy and clock drawing test). These data were later correlated with clinical and demographic characteristics.
Results: We selected 27 patients with PD and 13 with ET. FDS was more prevalent in PD patients (41% vs. 8%; p=0.028), with a sensitivity of 41% and specificity of 92%. PD patients traced a sun with a significantly smaller diameter and shorter rays. PD patients also drew a significantly smaller flower and shorter, flatter petals. Comparing patients with positive vs. negative FDS, we found that patients with a positive FDS scored less on the pentagons copy (5.0±1.9 vs. 6.0±1.1; p=0.025) and clock drawing test (5.0±2.6 vs. 9.0±2.8; p=0.045), with no significant differences in the MDS-UPDRS motor tasks.
Conclusion: Graphomotor tasks can be useful in the distinction of patients with PD and ET. The presence of FDS appears to be associated with visuospatial dysfunction, but not with motor symptoms.
Disclosure: Nothing to disclose.

EPO-441

Different stroke localizations presenting as astasia-abasia

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Background and aims: The concept of astasia-abasia encompasses the inability to maintain an upright position or to walk in someone with normal lower limb strength and without apraxia. Although classically associated with functional disorders, a similar phenomenology has been described in patients with stroke.
Methods: Description of two cases of astasia-abasia in patients with stroke of different etiologies and localizations.
Results: A 75-year-old male was admitted for gait impairment upon awakening. Neurological examination was unremarkable, namely in terms of strength, sensation, praxis and motor coordination. The CT-scan showed a left talamo-capsular hemorrhage. During hospitalization, even though the patient didn't develop new deficits, he was unable to maintain an upright position or to walk without support. A 73-year-old woman, with several vascular risk factors, was admitted for sudden inability to walk after a fall. When examined, she had no neurological deficits and looked like she was overstating her inability to walk. CT scan didn't show acute lesions. During hospitalization, she remained unable to stand and walk without support. An MRi was requested and showed a small ischemic lesion in the very distal left posterior cerebral artery territory.
Conclusion: While rarely, astasia-abasia can be the presentation of stroke. Recent reports revealed that the most frequent brain regions affected by structural causes of astasia-abasia are the thalamus, namely, the superior portion of the ventro-lateral nucleus, and the cingulus. Given its frequent association with functional disorders, we found relevant to alert to the differential diagnosis of this clinical phenomenon, particularly in patients with vascular risk factors.
Disclosure: The authors have nothing to disclose.

EPO-442

Study-Design to Assess the Effect of Opicapone on Levodopa PK at Different Levodopa-Optimized Treatment Regimens

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Background and aims: Opicapone (OPC), a once-daily (QD) catechol-O-methyltransferase inhibitor, proved effective in the treatment of end-of-dose motor fluctuations in Parkinson's Disease (PD) patients [1,2]. Levodopa (L-DOPA) is considered the gold standard treatment of PD, yet comes with side effects including motor fluctuations and dyskinesia. Therefore, many physicians follow a dopa-optimization strategy. This study was designed to assess the effect of OPC 50mg QD on L-DOPA pharmacokinetics (PK) in different L-DOPA/Carbidopa (LD/CD) treatment-optimized regimens in patients with end-of-dose motor fluctuations.
Methods: 24 medically stable PD patients with a total daily LD/CD dose of 500/125mg [preferred on five administrations per day (Q5)]. From enrolment (V2) up to 14±2 days, a LD/CD-reference treatment of 100/25mg LD/CD Q5 (500/125mg total daily dose) will be applied. At baseline (V3), patients will be equally randomized to: • Q4 LD/CD-regimen of 400/100mg total daily dose plus OPC 50mg • Q5 LD/CD-regimen of 400/100mg total daily dose plus OPC 50mg Patients will maintain the LD/CD regimen for up to 14±2 days (V4). PK assessments for LD/CD-reference will be performed at V3 and for both LD/CD+OPC regimens at V4 (Figure 1).

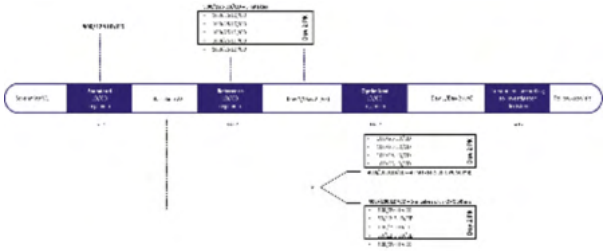

Figure 1. Overall study design. CD: Carbidopa, LD: Levodopa, PK: pharmacokinetics

Results: Primary endpoint will be PK based. Secondary endpoints include tolerability, functional motor assessments (subject diary charts for ON/OFF periods) and patient Global-Impression-of-Change scale (PGI-C). First-patient-in and last-patient-out are expected to 2021. Timelines might be impacted by COVID-19 pandemic situation.
Conclusion: This study will evaluate OPC effect on L-DOPA PK in different LD/CD treatment-optimized regimens in patients with end-of-dose motor fluctuations.
Disclosure: Nothing to disclose.

EPO-443

Opicapone EPSILON study in early Parkinson's: design of a phase III, double-blind, randomized, placebo-controlled study

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Background and aims: Opicapone (OPC) proved to be effective in the treatment of end-of-dose motor fluctuations in Parkinson's Disease (PD) patients [1,2]. When OPC is co-administered with L-dopa and dopa decarboxylase inhibitors (DDCis), peripheral COMT is inhibited increasing L-dopa bioavailability. This study aims to explore the potential of OPC to enhance the clinical benefit of L-dopa/DDCi in early-stage PD on stable treatment.
Methods: Patients (aged 30–80 years) with idiopathic PD, treated with 3–4 daily oral doses of up to 500mg L-dopa, with signs of treatable motor disability but no motor complications will be randomised in a 1:1 ratio to receive OPC 50mg once-daily or placebo during a 6-month double-blind evaluation-period. Subject's L-dopa/DDCi regimen should remain stable throughout the double-blind period. At the end of the double-blind period, subjects may enter an additional 1-year, open-label period of OPC 50mg treatment (Figure 1). 162 subjects in each group is necessary to detect a minimum clinically relevant magnitude of effect between arms.

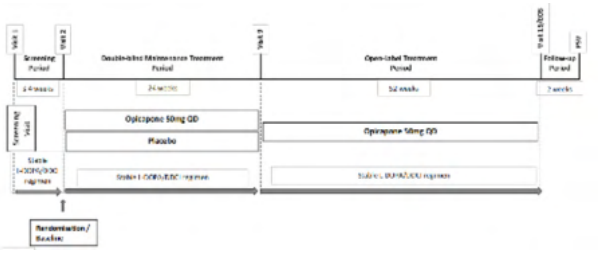

Figure 1. Overall EPSILON study design. EOS = End-of-Study Visit; DDCI = dopa decarboxylase inhibitor; L DOPA = levodopa; PSV = Post-Study Visit; QD = once daily

Results: Change from baseline in MDS-UPDRS Part III is the primary endpoint. Secondary endpoints include tolerability, functional motor and non-motor assessments (MDS-UPDRS, NMSS, PDQ-39, PDSS-2) and Global Impression of Change scales (CGI-C, PGI-C). First-patient-in is expected for early 2021 and Last-patient-out from double-blind in late 2022. Timelines might be impacted by COVID-19 pandemic situation.
Conclusion: This study will evaluate the efficacy of once-daily OPC 50mg as add-on to stable L-dopa/DDCi therapy in patients with early-stage PD.
Disclosure: 1. Ferreira et al., Lancet Neurol. 2016;15(2):154-165; 2. Lees et al., JAMA Neurol. 2017;74(2):197-206.

EPO-444

Opicapone ADOPTION study in Parkinson's: design of a randomized prospective, open-label exploratory trial

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Background and aims: Opicapone (OPC) proved to be effective in the treatment of end-of-dose motor fluctuations in Parkinson's Disease (PD) patients [1,2]. About 50% of PD patients within 2–5 years, and 80–100% patients within 10 years of L-dopa therapy, show some degree of motor complications [3,4]. Subsequently, the standard approach is to alter the L-dopa dosing regimen, either by increasing the dose or by 'fractionating' its total daily dose [5]. This study aims to explore the potential of OPC to optimize L-dopa/DDCi as first line approach to treat wearing-off.

Methods: Approximately 100 patients (aged 30 years) with idiopathic PD, treated with 3–4 daily oral L-dopa doses up to 600mg, and signs of wearing-off (<2 years) will be equally randomised to receive OPC 50mg once-daily or 100mg L-dopa/DDCI during a 4-week open-label evaluation-period (Figure 1).

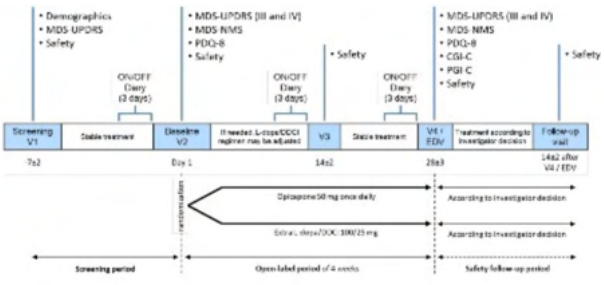

Figure 1. Overall ADOPTION study design
CGI-C: Clinical Global Impression of Change; EDD: Early Study Discontinuation; MoCA: Montreal Cognitive Assessment; PDQ-8: Parkinson's Disease Questionnaire 8-Item; PGI-C: Patient Global Impression of Change; UPDRS: Unified Parkinson's Disease Rating Scale

Results: Primary endpoint is the change from baseline in OFF-time. Secondary endpoints include tolerability, functional motor and non-motor assessments (MDS-UPDRS, MDS-NMS, PDQ-8, Hauser's home diary) and Global Impression of Change (CGI-C, PGI-C). As this is an descriptive/exploratory study, no formal sample size calculation was performed. Study sites are in Germany, Italy, Portugal, Spain and UK. First-patient-in is expected for 2021 and Last-patient-out to late 2022. Timelines might be impacted by COVID-19 pandemic situation.

Conclusion: This study will evaluate the potential of OPC to optimize L-dopa/DDCi as first line approach to treat wearing-off.

Disclosure: 1.Lancet Neurol. 2016;15(2):154-165; 2.JAMA Neurol. 2017;74(2):197-206; 3.Journal Neurol. 2019; 266:2164-2176; 4.Expert Opinion on Pharmacotherapy. 2019;20(18):2201–2207; 5.Neuropsychiatric Disease and Treatment. 2008;4(1):39–47

EPO-445

A misdiagnosed case of Juvenile Parkinsonism with infantile onset due to Parkin mutation

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Background and aims: Juvenile Parkinson's disease (JP) is a rare, very early presentation of Parkinson disease (PD), manifesting before the age of 21 and associated with mutations in the PARK2 gene. Unlike late onset idiopathic PD, JP may manifest with atypical features, such as dystonia, subtle pyramidal signs and psychiatric disturbances. Herein, we report a unique case of JP with unknown family history (she had been adopted after being abandoned soon after birth).

Methods: A three years-old girl developed a slowly progressive gait disorder with clumsiness and unsteadiness, as well as lower limb stiffness with frequent falls. Given the presence of speech problems she was considered affected by intellectual disability and initially misdiagnosed as cerebral palsy. No other focal neurological signs were reported at that time. At the age of 4, a trial with levodopa was initiated with some benefit. When she was 30, stiffness spread also to the upper limbs. At the age of 39 she was wheelchair-bound. She came to our attention when she was 49. Neurological examination revealed cervical dystonia, dystonic postures of upper limbs, moderate bradykinesia, diffuse plastic rigidity, ballistic movements in her legs and pyramidal signs. Brain MRI performed under sedation was normal and ruled out perinatal injuries.

Results: A multigen panel revealed a homozygous mutation in PARK 2 gene, NM_004562.2: c.823C&g>T p.(Arg 275 Trp).

Conclusion: JP related to PARK2 mutation may occur even during infancy. Our case underlines the importance of considering JP also in a very young child presenting with dystonia, gait and balance problems and some levodopa responsiveness.

Disclosure: We declare that we have no conflict of interest.

EPO-446

Acute Onset Adulthood Reversible Chorea Associated With Vitamin B12 Deficiency

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Background and aims: Vitamin B12 deficiency is a metabolic disorder which commonly manifests with a subacute combined degeneration of the spinal cord, dementia, optic atrophy, or psychiatric disorders. However, it is unusually revealed by movement disorders. These latter are described in about 50% of pediatric cases of vitamin B12 deficiency, but they remain rare and unrecognized in adults.
Methods: A case report.
Results: A 55-year-old man presented with a 3-month history of gait disturbance, postural instability and limbs paresthesia. Three weeks before admission to our department, he developed involuntary movements in an upper limb. Clinical examination revealed a combined degeneration of the spinal cord syndrome, associated with a combination of tremor and chorea in the right upper limb. Magnetic resonance imaging (MRI) showed subcortical white matter, basal ganglia, and spinal posterior columns hyperintense lesions on T2-weighted and FLAIR images. A complete etiological workup had revealed a severe cobalamin deficiency with a high level of homocysteine. After sufficient cobalamin substitution, all symptoms significantly regressed.
Conclusion: Neurologic manifestations of vitamin B12 deficiency are heterogeneous, misleading the diagnosis in many cases. It should be evoked even in acute onset chorea, allowing an early treatment initiation with a possible full reversibility of symptoms.
Disclosure: Nothing to disclose.

EPO-447

Depression mostly predict quality of life in focal and segmental dystonia patients

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Background and aims: Dystonia is movement disorder presented with involuntary muscle contraction causing abnormal posture, movement or both. Beside motor symptoms patients may also report nonmotor symptoms such as depression, anxyety, fatigue, sleep disorder and cognitive impairment. Both, motor and nonmotor symptoms, influence negatively on patients quality of life (QoL). We aim to predict which nonmotor symptom (depression, anxyety, sleep problems, daily sleepiness) influence most on dystonia patients QoL.
Methods: Demographic data (sex, age and disease duration) were collected from patients medical documents. Patients were survey for nonmotor symptoms using Fatigue Assessment Scale, Beck Depression Inventory II, Beck Anxyety Inventory, Pittsburg Sleep Questionairre Index and Epwort Sleep Scale. Quality of Life was assessed using Short Form Survey 36 that measure nine component of QoL.
Results: Sixty patients (43 female and 17 male) with focal and segmental dystonia were evaluated. Daily sleepines negatively correlate with all nine components of QoL, while depression, anxyety and sleep disturbances negatively correlate with eight components, beside health change. A multipe regression was run to predict which nonmotor symptom mostly predict each QoL component. Daily sleepines predict mostly physical functioning ($p=0.009$); depression predict mostly emotional role functioning ($p=0.024$), energy ($p=0.003$), emotion ($p<0.001$), social role functioning ($p=0.03$) and general health ($p=0.01$); fatigue predict mostly energy ($p=0.044$); and anxyety predict mostly social role functioning ($p=0.027$).
Conclusion: All nonmotor symptoms negatively correlate with QoL components, but depression predict most QoL components.
Disclosure: Nothing to disclose.

EPO-448

Gastric duodopa infusion in three patients with percutaneus endoscopic tube complications

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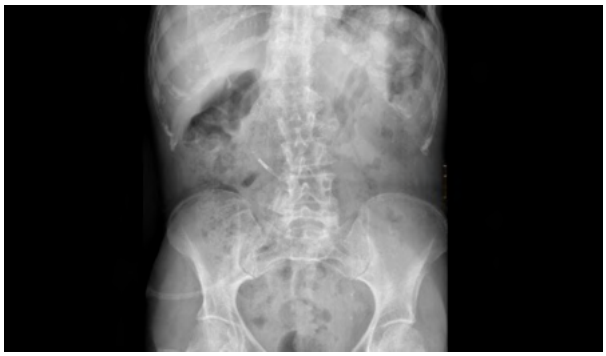
Background and aims: Patients at late stage of Parkinson's disease (PD) develop several motor and no motor fluctuations. Aim of this enteral administration of levodopa/carbidopa (LD/CD) is to bypass gastric administration and release directly in duodenum/jejunum a continuous levodopa flow. It improves quality of life and motor fluctuations. Adverse events related with the percutaneous gastrojejunal tube sometimes lead to treatment discontinuation. Tube's surgical placement directly into jejunal position has been proposed, but there is very low experience and high surgical risks. We figured out direct gastric administration of LD through percutaneous endoscopic gastrostomy (PEG).

Tube kinking



Tube kinking

Methods: Report an alternative way of enteral levodopa (LD) administration in three patients with local adverse effects related to duodenum tube.
Results: With continuous gastric LD/CD infusion patients maintained motor benefit and physical independence for the most activities until today (at least one year since the change of LD administration way). No new enteral adverse events related to gastric tube were reported.
Conclusion: The LD/CD enteral infusion has several well-known gastrointestinal adverse events peri-procedural and device-related. Adverse events related to the tube's distal end are lead to treatment discontinuation or fatal prognosis. Some authors use direct gastric infusion of LD/CD removing the jejunal accessory tube and leaving the PEG tube. This way of infusion has more motor fluctuations and less dose-benefit from extra doses than standard duodenal release, but it still has better outcomes and less dyskinesias comparing with oral levodopa.
Disclosure: All authors declare no conflict of interest.

EPO-449

Memantine-induced myoclonus: case report and literature review

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Background and aims: Myoclonus is a sudden, brief involuntary movement caused by muscle contraction or inhibition. It has multiple aetiologies, including neurodegenerative diseases and epilepsy and is frequently drug-induced.
Methods: Case report (with video) and literature review.
Results: 89-year-old woman with Parkinson's disease dementia, admitted to the emergency department with a 2-week history of progressively worsening abnormal movements. She had been started on memantine one month earlier, with progressive dose increment. Physical examination was significant for synchronized brief, involuntary, sudden jerks of all four limbs, face, and tongue, both positive and negative, along with guttural sounds. These were not present at rest and were triggered by somaesthetic stimuli (touch), posture, action, and passive movement. Blood chemistry was unremarkable, head CT-scan was only positive for generalized cerebral atrophy and EEG was not available. These movements were interpreted as subcortical myoclonus. Memantine was stopped on the same day, and clonazepam and levetiracetam were started. Myoclonus resolved one day after memantine withdrawal and did not recur after clonazepam and levetiracetam were tapered down. The Naranjo Adverse Drug Reaction Probability Score was 4, suggesting that myoclonus was a possible adverse reaction to memantine.
Conclusion: Memantine is a N-methyl D-aspartate (NMDA) receptor antagonist that blocks the pathological activation of NMDA receptor. Literature review yielded seven case reports of memantine-induced myoclonus. All individuals were elderly with dementia. The onset of myoclonus ranged from six days to two months after memantine exposure, with complete resolution of myoclonus upon memantine cessation. A serotoninergic mechanism related to NMDA inhibition may underlie memantine-induced myoclonus.
Disclosure: Nothing to disclose.

EPO-450

DNA methylation signatures associated with the phenomenon of inverse comorbidity of Huntington disease and cancer

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Background and aims: The phenomenon of inverse comorbidity between Huntington disease (HD) and cancer is enclosed by reduced cancer incidence in HD patients. Previously, using the gene network reconstruction, we have identified candidate genes of this inverse comorbidity (APOE, PSEN1, INS, IL6, SQSTM1, SP1, HTT, LEP, HSPA4, BDNF). We proposed that altered DNA methylation of these genes is one of the key epigenetic events that contribute to the inverse comorbidity of HD and cancer.
Methods: DNA was extracted from whole blood of subjects with HD (n=17, aged 61.0±8.5 years), lung cancer ((LC) n=9, aged 59.9±6.3 years) and healthy individuals (HC) (n=14, 65.6±8.1 years). DNA methylation pattern was assessed using targeted bisulfite high-throughput seqeuncing on MiSeq System (Illumina). We analyzed CpG-sites (CpGs) located predominately in CpG-islands within the promoters of candidate genes: SP1 (10 CpGs), HTT (32 CpGs), LEP (31 CpGs), HSPA4 (40 CpGs), APOE (37 CpGs), BDNF (22 CpGs).
Results: We identified differential DNA methylation between three experimental groups for individual CpGs of SP1 (chr12:53772929; chr12:53772969; chr12:53773021; chr12:53773040 ; chr12:53773048; chr12:53773056; chr12:53773108) and HTT (chr4:3076345; chr4:3076351; chr4:3076357; chr4:3076537). Genome coordinates are given according to assembly GRCh37/hg19.
Conclusion: HTT and SP1 genes comprise promising targets for further research in the context of inverse comorbidity of HD and cancer. This study was supported by the Russian Foundation for Basic Research (project No. 19-015-00391, "Epigenetic Mechanisms of Tumor Suppression in Patients with Huntington's Disease").
Disclosure: Nothing to disclose.

MS and related disorders 3

EPO-451

The correlation between fatigue and sleep parameters in Multiple Sclerosis patients

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Background and aims: Poor sleep in Multiple Sclerosis (MS) patients is common and known as a possible cofounder of fatigue. For a better understanding of sleep-related problems in MS-patients, the aim of this research was to investigate the correlation between subjective and objective sleep measures and fatigue.
Methods: 20 MS patients, who were enrolled in a randomised controlled trial investigating the effects of bright light therapy on fatigue, were included in this analysis. Fatigue was assessed with the Fatigue Severity Scale (FSS). At baseline all study participants were screened for sleep disorders using the Pittsburgh Sleep Quality Index (PSQI), ambulatory polysomnography and sleep diaries.
Results: We did not find a significant correlation between FSS scores and PSQI scores or polysomnographic parameters (percentage of N2, N3 or REM sleep and wakefulness after sleep onset) in our sample. Subjective sleep onset latency and sleep duration assessed by sleep diaries over the course of six weeks correlated significantly with each other ($r=-0.18$, $p<0.01$) and with the restorative quality of sleep ($r=0.3$, $p<0.01$ and $r=-0.24$, $p<0.01$, respectively).
Conclusion: Neither subjective nor objective sleep parameters did correlate with the level of fatigue, but sleep was perceived as more refreshing if sleep onset was faster and sleep duration longer in our sample of MS patients.
Disclosure: Funded by Oesterreichische Nationalbank (OeNB). No other conflicts of interest.

EPO-452

Multiple sclerosis and ankylosing spondylitis: a case report

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Background and aims: Multiple sclerosis (MS) is a chronic autoimmune neurodegenerative central nervous system disease. Ankylosing spondylitis (AS) is a chronic inflammatory autoimmune disease that mainly affects spine joints. Coexistence for these two diseases is described with paucity.
Methods: In 2019, a 30-year-old man complained about tingling in the left IV and V fingers, lower arm, and leg. After receiving methylprednisolone, his condition improved. He was diagnosed with MS and received dimethyl fumarate, but four months later he complained of tingling and pain in lumbar and thoracic region. Neurological examination revealed mild instability in the Romberg test and tandem gait. The patient was prescribed etoricoxib, tizanidine, amitriptyline, gabapentin. Despite therapy, two months later pain remained at night. Dexamethasone was prescribed. MRI revealed the seronegative spondyloarthropathy, bilateral active sacroiliitis which led to diagnostic of AS. Considering that nonsteroidal anti-inflammatory drugs were inefficient and TNF alfa inhibitors are contraindicated in patients with MS, IL-17 blocker Secukinumab was prescribed. Dimethyl fumarate therapy was discontinued.
Results: Secukinumab therapy provided clinical stability of two autoimmune comorbidities.
Conclusion: It is necessary to collaborate with colleagues and to diagnose the concomitant disease as fast as possible to find a specific, safe and effective therapy to achieve clinical stability.
Disclosure: Nothing to disclose.

EPO-453

Alemtuzumab associated dermatitis

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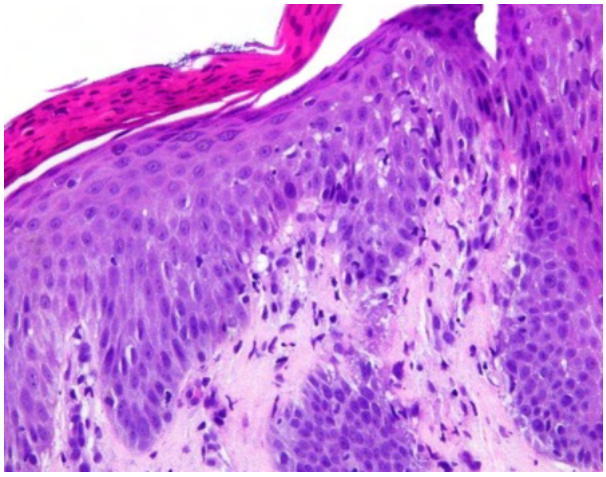
Background and aims: Alemtuzumab is a monoclonal antibody directed against CD 52. Clark et al. identified five patients with cutaneous T-cell lymphoma (CTCL) or chronic lymphocytic leukemia (CLL) treated with alemtuzumab who subsequently developed widespread dermatitis. The hypothesis was postulated that anti-CD 52 antibodies deplete circulating central memory T-cells more effective than non-recirculating resident memory T cell and the resultant immunomodulation may cause inflammatory dermatoses.

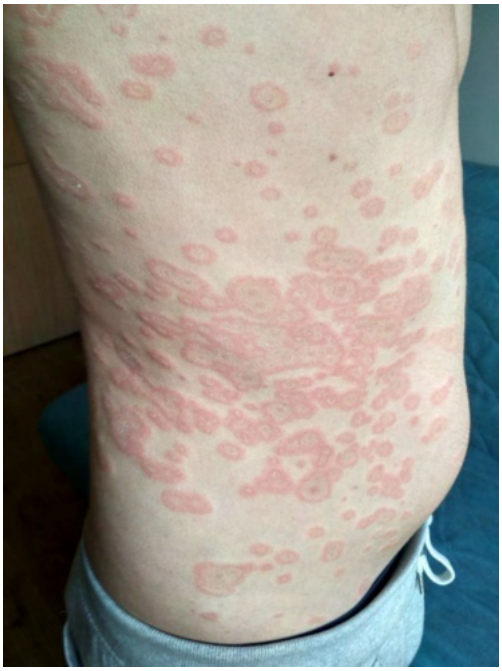
Methods: We present a case of 27-years old male with multiple sclerosis, treated with alemtuzumab. Patient developed non-pruritic, erythematous plaques on the chest, back, and extremities. Clinical and histopathological review of the findings was performed, and compared with the data obtained by Clark et al.

Results: Patient received 12mg of alemtuzumab daily for five consecutive days (total 60mg), followed 12 months later by 12 mg daily for three consecutive days (total 36 mg). After every infusion widespread multiple lesions were observed and persisted for three months. The patient received trimetoprym and acyclovir prophylaxis for six months. There was no improvement after fexofenadin and low doses of steroids. Skin biopsy was performed two months after second infusion. Histologic examination revelaed epidermal spongiosis with focal parakeratosis and lymphocytic exocytosis, focal interface dermatits of vacuolar type with perivascular lymphocytic infiltration.



Histopathology showed spongiotic dermatitis with multifocal parakeratosis.

Conclusion: The data suggest the existence of novel hypersensitivity reaction due to immunologic reaction precipitated by the persistence of resident memory T-cells in the skin. References: Clark SL et al. Histopathologic spectrum of hypersensitivity reactions associated with anti-CD52 therapy (alemtuzumab). J Cutan Pathol. 2016.



Well-demarcated, multiple erythematous plaques.

Disclosure: Nothing to disclose.

EPO-454

Cognitive impairment in multiple sclerosis in daily clinical practice using the SDMT and conventional MRI

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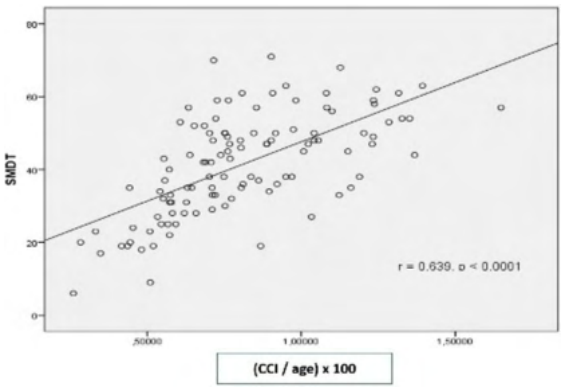
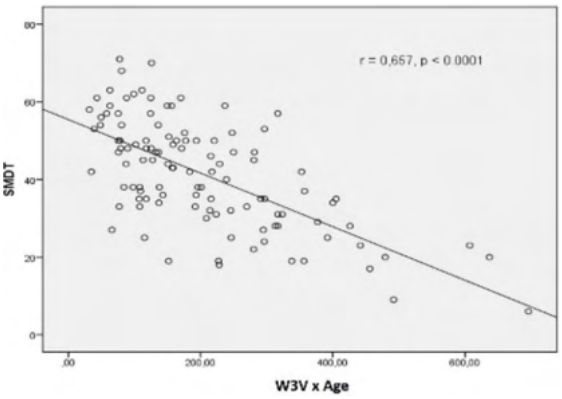
Background and aims: Cognitive impairment is common in multiple sclerosis (MS), is correlated with different measures of brain atrophy, and has a negative impact on social, family and work life. The way to study this cognitive impairment in daily clinical practice involves using simple tests such as the SDMT and obtaining data on brain atrophy from conventional magnetic resonance imaging (MRI). Our objective was to assess cognitive impairment and its correlation with two-dimensional measures of brain atrophy on MRI.

Methods: 113 patients with relapsing remitting MS were studied. All patients were administered the SDMT. As measures of brain atrophy, the corpus callosum index (CCI) and the width of the third ventricle (W3V) were calculated. Pearson's r was used for correlations.

Results: The raw SDMT scores were significantly correlated ($p < 0.001$) with age ($r=-0.58$), EDSS ($r=-0.49$), CCI ($r=0.43$), and W3V ($r=-0.57$). The measures of brain atrophy in our study showed a high correlation between them ($r=-0.72$, $p<0.0001$). By including age in the measures of brain atrophy, the correlations improved: CCI/Age ($r=0.63$, $p<0.001$) and W3VxAge ($r=-0.66$, $p<0.0001$).



Correlation between SDMT score and the corpus callosum index (CCI/Age)



Correlation between SDMT score and the width of the third brain ventricle (W3V x Age)

Conclusion: In daily clinical practice, the SDMT is a good screening tool for cognitive impairment in MS and has a moderate correlation with disability (EDSS) and a high correlation with measures of brain atrophy.

Disclosure: The author declares that there are no conflicts of interest.

EPO-455

BTK Inhibitor Tolebrutinib in Patients With Progressive MS: Design of Phase 3 PERSEUS and HERCULES Trials

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Background and aims: Progressive multiple sclerosis (MS) presents a significant unmet need. Tolebrutinib is an oral, central nervous system–penetrant, irreversible Bruton's tyrosine kinase inhibitor with the potential to affect both adaptive and innate immunity. It may modulate chronic inflammatory activity driven by activated microglia, a common feature of progressive MS. Here we describe the design of two phase 3 tolebrutinib trials, PERSEUS (NCT04458051) and HERCULES (NCT04411641), in patients with primary progressive (PPMS) and nonrelapsing secondary progressive MS (NR-SPMS), respectively.

Methods: Trial protocols were developed based on tolebrutinib pharmacologic profile, phase 2b trial (NCT03889639) results, and knowledge from previous trials in progressive MS.

Results: PERSEUS (planned enrolment: 990 patients with PPMS) and HERCULES (planned enrolment: 1290 patients with NR-SPMS) are randomized (2:1), double-blind, placebo-controlled, parallel-group, multicentre trials. They will evaluate efficacy and safety of tolebrutinib (once daily) over the variable, event-driven period of 2448 months. Primary endpoint in both trials is time to onset of 6-month confirmed disability progression. Secondary endpoints include clinical and MRI assessments and safety/tolerability evaluation. Exploratory endpoints, expected to provide additional evidence for tolebrutinib activity on neuroinflammation and neurodegeneration, include assessments of chronic active lesions (slowly expanding lesions and phase rim lesions). Enrolment in both trials began in August–September 2020.

Conclusion: The PERSEUS and HERCULES phase three trials will assess efficacy and safety of tolebrutinib in patients with progressive MS. Exploratory endpoints will assess the effect of tolebrutinib treatment on chronic active lesions, which are associated with activated microglia and with disability accumulation and progression in MS.

Disclosure: STUDY SUPPORT: Sanofi.

EPO-456

The Portuguese Multiple Sclerosis Observatory: Resource Tool for Measuring and Improving Outcomes in Multiple Sclerosis

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Background and aims: Several registries and international registry networks have been launched over last years significantly raising the knowledge and research in multiple sclerosis (MS). The Portuguese MS Observatory was conceptualized by Grupo de Estudos de Esclerose Múltipla (GEEM) to track information regarding patient characterization, disease course, functional and cognitive status, treatment pathway, effectiveness and safety of MS treatments in Portugal.

Methods: The Portuguese MS Observatory is a national, prospective, multicenter, observational system operating in Portuguese NHS hospitals with continued neurological care. Five-year retrospective data of existing patients will be collected from clinical charts and updated prospectively. Data from newly diagnosed patients will be prospectively collected. Assessments include demographics, past and current DMTs, concomitant medication, relapses, MRI, expanded disability status scale (EDSS), symbol digit modalities test (SDMT), MS functional composite (MSFC), neurofilament levels and adverse events. Follow-up is 25 years from enrollment or until death, whichever occurs first.

Results: The registry will be launched in 2021 in six hospitals. First data cut-off analysis is planned for second quarter of 2021 aiming to characterize the first hundred patients enrolled in the registry. New data modules may be added to the registry to track innovative measures like OCT and serum/CSF biomarkers.

Conclusion: The Portuguese MS Observatory is an unique longitudinal real-world data source allowing short and long-term assessment of outcomes and extended evaluation of emerging MS treatments, including high efficacy treatments. This registry will increase the knowledge of healthcare professionals, decision-makers and patients around the Portuguese MS treatment landscape and ultimately overcome challenges in MS management.

Disclosure: No disclosures.

EPO-457

Claims-based algorithms to identify NMOSD patients and relapses in German claims data

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[1] F. Hoffmann-La Roche Ltd, Basel, Switzerland, [2] Ingress-Health HWM GmbH, Wismar, Germany

Background and aims: Neuromyelitis optica spectrum disorder (NMOSD) is a rare autoimmune condition, often misdiagnosed as multiple sclerosis. Unfortunately, International Classification of Diseases (ICD) codes alone are limited in their capacity to successfully identify NMOSD patients and relapses. The aim of this study was therefore to develop identification algorithms using a German insurance claims database.
Methods: Based on a prior systematic literature review (ISPOR Europe 2020 PRO138), 12 patient identification algorithms and two relapse detection algorithms were developed and indirectly assessed using patient characteristics. The algorithms differed in NMOSD-associated symptom codes, number of required codes, and type of diagnosing physician. Relapses were identified according to symptom codes and subsequent acute treatment claims.
Results: Sample sizes for the tested algorithms ranged from 19–41 patients, resulting in NMOSD prevalence rates of 0.84–1.28 per 100,000. Inclusion of symptom codes other than neuromyelitis optica (NMO) (e.g., optic neuritis) had minimal impact, whereas the number of NMO codes and the type of diagnosing physician had greater influence. Depending on the applied algorithm, the mean age of patients was 50–59 years, and 53–67% of patients were female. The relapse identification algorithms yielded annualised relapse rates (ARR) of 0.14 and 0.38, using a 7-day window and no time limit between the symptom code and acute treatment claim, respectively.
Conclusion: The evaluated algorithms detected cohorts with anticipated demographics and disease prevalence, however, relapse identification yielded a lower-than-expected ARR. External validation against medical charts, and the inclusion of additional data, e.g., aquaporin-4 immunoglobulin G serostatus, are recommended to reinforce these findings.
Disclosure: Funded by F. Hoffmann-La Roche. Writing and editorial assistance was provided by Abi Heffer of ApotheCom, London, UK.

EPO-458

2 cases of Relapsing-Remitting Multiple Sclerosis with Baló-like lesions treated with Natalizumab

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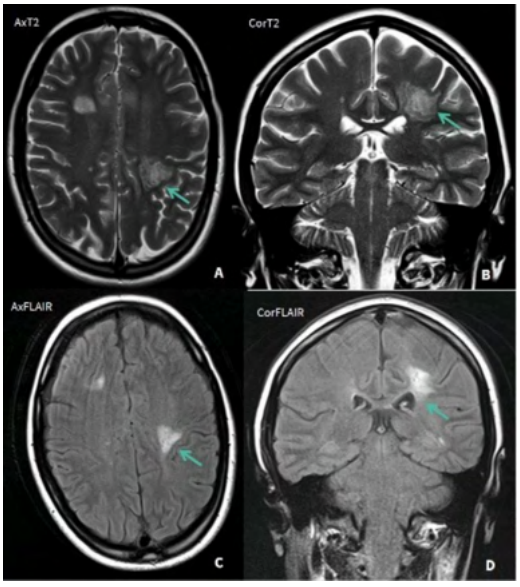
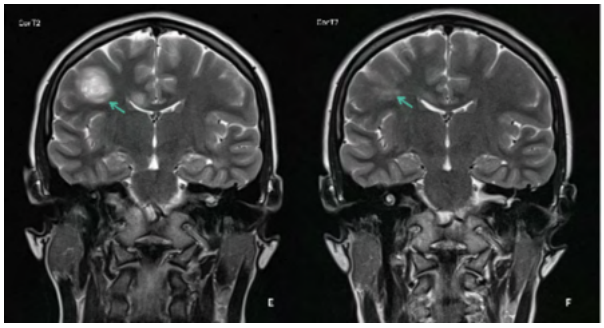
Background and aims: Baló's concentric sclerosis (BCS) was described as a rare and fatal variant of multiple sclerosis (MS). The advent of MRI showed that BCS lesions and lesions with intermediate characteristics (Baló-like) may appear during conventional MS disease course. It is considered reasonable that patients with atypical lesions that meet criteria for MS should initiate disease-modifying therapy (DMT), but currently evidence to guide the treatment of these patients is lacking.
Methods: Series of two cases.
Results: Two 28 and 34 years-old women, presenting with aggressive inaugural attacks, with incomplete recovery with corticosteroids and in one case with added plasmapheresis. MRI documented (case 1): an enhancing left peri-rolandic subcortical Baló-like lesion, a right frontal lesion with grossly concentric pattern, other demyelinating lesions including periventricular and an enhancing spinal cord lesion; (case 2): two enhancing Baló-like lesions (right justacortical frontal and right subcortical parietal), and other demyelinating periventricular lesions. Both patients had type 2 CSF IgG oligoclonal bands, negative anti-AQP4 and anti-MOG antibodies. Relapsing-remitting MS with high disease activity was diagnosed, and Natalizumab was started (baseline EDSS 3.0 and 3.5) with positive evolution of BCS lesions and no clinical or MRI activity at one year follow-up (last EDSS 2.0 and 2.5, respectively).



Case 1 initial MRI (A and B) showing a left peri-rolandic subcortical Baló-like lesion (arrow) and a right frontal lesion with grossly concentric pattern; and one year post Natalizumab control MRI (C and D) showing favourable evolution of Baló-like lesion.



Case 2 initial MRI (E) showing a right justacortical frontal Baló-like lesion (arrow); and one year post Natalizumab control MRI (F) showing favourable evolution of Baló-like lesion (arrow) with reduction of T2 hyperintensity and tumefactive appearance.

Conclusion: We describe two atypical MS cases presenting with BCS lesions, treated with Natalizumab for one year, with good clinical and MRI outcomes. There are currently no guidelines or randomized controlled trials to guide DMT in this group of patients. Natalizumab could be a viable option and deserves more investigation.
Disclosure: Nothing to disclose.

EPO-459

Brief International Cognitive Assessment for MS (BICAMS) accurately captures clinically meaningful cognitive impairment

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Background and aims: The Brief International Cognitive Assessment for MS (BICAMS) was created as a brief instrument for the evaluation of cognitive impairment in multiple sclerosis (MS). Despite being a validated and standardized screening tool, data is lacking regarding its ecological validity, that is the degree to which BICAMS performance predicts meaningful outcomes in real-world settings.
Methods: 60 MS patients and sixty healthy controls were enrolled. All participants underwent BICAMS testing, MS International Quality of Life questionnaire (MusiQoL) assessment and 3Tesla brain MRI. Group comparisons were performed using Chi-Square test and t test for unpaired samples.
Results: Patients with MS had significantly lower scores on all BICAMS cognitive domains compared to HC ($p<0.001$). 13 MS patients (21.7%) were classified as cognitively impaired. 10 (76.9%) MS patients with cognitive impairment were unemployed (versus 25.5% in cognitively preserved patients, $p=0.001$), supporting a significant association between BICAMS performance and employment status. Considering patient-reported quality of life, cognitively impaired MS patients had significantly lower MusiQoL scores compared to cognitively preserved MS patients (53.3 vs 64.0, $p=0.014$). Regarding MRI measures of brain atrophy, MS patients with cognitive impairment had lower subcortical grey matter volume (3.05 ± 0.58 vs 3.43 ± 0.38, $p=0.008$) and thalamus volume (0.37 ± 0.08 vs 0.42 ± 0.06, $p=0.028$). Also, cognitively impaired patients had significantly higher T2 lesion load (26.8 ± 21.6 vs 14.0 ± 12.6, $p=0.008$).
Conclusion: This study shows that BICAMS is a valid cognitive assessment tool in real-life settings, predicting employment status and quality of life. Furthermore, BICAMS performance was associated with subcortical brain atrophy, in particular thalamus atrophy, and higher lesion load.
Disclosure: The authors report no disclosures.

EPO-460

A Patient-based Digital Tool to Detect Early Signs of Changes in MS Symptoms and Progression: Your MS Questionnaire

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Background and aims: While evaluating MSProDiscuss™, development of a patient-completed tool was a common recommendation to monitor experiences of people with multiple sclerosis (pwMS) over time and facilitate discussions with health-care professionals (HCPs). Your MS Questionnaire (YourMSQ) was developed to be completed by pwMS. Here we evaluate its usability to help both pwMS and HCPs understand changes in MS-symptoms, disease progression, and their impact on daily activities.

Methods: YourMSQ is derived from MSProDiscuss, using input from pwMS, patient organizations and HCPs to include feedback from a broad-range of RRMS/SPMS patients. Asking 15 questions, it captures the perception of pwMS regarding changes in MS-symptoms, disability progression and impact on daily-living over past 6-months. To assess YourMSQ, two surveys (15 questions each) are being conducted among treating neurologists initially after every consultation to understand patient-details, patient-satisfaction, HCP-satisfaction, and again after up to 40 consultations (minimum 10 consultations required). This will capture in-depth feedback on usefulness, integration in clinical practice in addition to MSProDiscuss, and improvement areas. PwMS were given the choice of an electronic or paper version of the questionnaire.

Results: Testing of YourMSQ is currently ongoing across eight countries (US, UK, Germany, Spain, Italy, Canada, Australia and China), permitting assessment of different aspects of its usability. Results will be presented at the meeting.

Conclusion: YourMSQ will collect real-world feedback from pwMS and help neurologists manage MS-disease activity and symptoms in daily-life. When completed before consultations, it may benefit pwMS and physicians through (1) a better-structured conversation and (2) potential use in telemedicine.

Disclosure: The study was supported by Novartis Pharma AG, Switzerland.

EPO-461

Spastic dystonia in multiple sclerosis: the dark side of muscle hypertonia

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Background and aims: Surface EMG (sEMG) can show that spasticity and spastic dystonia (SD) can present velocity dependent muscle hypertonia. The study aims to investigate prevalence of SD in hypertonic muscles of patients with Multiple Sclerosis (PwMS).
Methods: PwMS with velocity dependent hypertonia affecting at least one joint among elbow, wrist, knee and ankle. Scales administered: Modified Ashworth Scale, Medical Research Council, pain and spasticity NRS, Multiple Sclerosis Impact Scale. To investigate tonic stretch reflex (TSR) and static stretch reflex (SSR), EMG activity was investigated in rest position and in response to a manually performed passive stretch.
Results: Among 108 hypertonic muscles, 95 were lower limb muscles: 76 were extensors and 19 flexors. Among upper limb, 11 were flexors and two extensors. TSR was detected in 104 muscles, confirming that in PwMS, hypertonia has a reflex component in most of affected muscles. TSR-alone was predominant EMG pattern in extensor, while SSR was prevalent in flexor. SD was evenly distributed in flexor and extensor, prevalent in upper limb. The size of TSR was always greater in muscles with SD than in muscles with spasticity. In flexor, EMG pattern TSR+SSR was characterised by larger TSR than in spasticity, and similar to SD. In extensor same EMG pattern had TSR of similar size of that in spasticity, smaller than in SD. In flexors, SSR always accompanied SD.
Conclusion: Spasticity (TSR-alone) predominates in extensors muscles, with higher frequency of SSR in flexors, reflecting increased spinal excitability of stretch reflex circuitry. SD reflects increased stretch reflex excitability in flexor and extensor.
Disclosure: Founded by Italian Multiple Sclerosis Foundation.

EPO-462

Patient-reported Outcomes used in Multiple Sclerosis Trials: Critical Assessment and Insights from People Living with MS

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Background and aims: Regulatory guidance recommends that patient-reported outcomes (PROs) are defined by clinical and patient-relevant conceptual frameworks. Four PROs measuring quality of life (QoL) and fatigue commonly used, or recently developed for use, in MS trials were assessed as to whether they satisfy current guidance by appropriately measuring outcomes relevant to persons living with MS (PLwMS).
Methods: Information was extracted on domain definitions, items measured and conceptual frameworks from PROs measuring QoL (54-item MSQoL [MSQoL-54], Leeds MSQoL [LMSQoL]) and fatigue (Fatigue Symptoms and Impacts Questionnaire-Relapsing MS [FSIQ-RMS], modified Fatigue Impact Scale [mFIS]). Expert patients (EPs) provided PRO-related feedback through structured interviews. Seven EPs were interviewed (further interviews to be conducted).
Results: Of the PROs, only FSIQ-RMS was based on a conceptual framework. The 12-subscale MSQoL-54 provides two domain scores (physical and mental health), although these domains were not defined prospectively. However, EPs liked the ability to measure a holistic impact of MS. LMSQoL was developed with patient input; EPs liked its ease of use, but the domain (wellbeing/QoL) used correlation with other instruments for interpretation. The 20-item FSIQ-RMS, assessing physical and cognitive aspects of fatigue, was developed with patient involvement using current guidance but EPs preferred the more patient-friendly language of the 21-item mFIS. However, some mFIS items (e.g. poor coordination) are not fatigue-specific.
Conclusion: PROs lacked domain definitions and/or conceptual frameworks, limiting their validity/interpretation of results. Defining domains prospectively and involving PLwMS from the onset could yield PROs that better assess the symptoms and impact of MS in clinical trials and clinical practice.
Disclosure: The study was supported by Novartis Pharma AG, Switzerland. The detailed author disclosures will be presented in the subsequent presentation.

EPO-463

Development of an APP (ABOUTCOME) for evaluation in multiple sclerosis

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Background and aims: Data collection represents fundamental component of clinical research and practice, allowing evaluation of treatment efficacy and analysis of collected data. The aim of the study is to implement data collection through creation and validation of app ABOUTCOME, to allow data storage and facilitate patients to fulfil questionnaires.
Methods: ABOUTCOME has been developed for people with Multiple Sclerosis (PwMS), it consists of standardized tests and self-administered measures. Measures: Disability of the Arm Shoulder and Hand (DASH), Abilhand, Manual Ability Measure-36 (MAM-36), Fatigue Severity Scale (FSS), Modified Fatigue Impact Scale (MFIS), Modified Ashworth Scale (MAS), 9-Hole Peg Test (9-HPT), Hand Grip Strength (HGS), Expanded Disability Status Scale (EDSS), Brief International Cognitive Assessment Multiple Sclerosis (BICAMS). ABOUTCOME is multilanguage (Italian and English), with available users' manual.
Results: 16 PwMS [10 female, mean age 58.2 years (DS=7.71), mean EDSS 6.5 (DS=0.98), three relapsing remitting MS, 13 progressive MS] completed five self-administrated scales (DASH, Abilhand, MAM-36, FSS, MFIS) on paper and tablet version. An ad hoc questionnaire has been created to evaluate necessary commitment to complete questionnaires, mental fatigue and frustration level due to paper and tablet implementation.
Conclusion: 14 MS subjects preferred and considered less challenging tablet compilation. The possibility to use a simple finger tap rather than pencil pinch has proved to be good alternative, reducing the effort of subjects and the time employed. Data export and database creation directly from ABOUTCOME resulted easier and more immediate, removing paper transcription errors. ABOUTCOME is available on Android systems and can be implemented including other evaluation measures.
Disclosure: The study was funded by Italian Multiple Sclerosis Foundation.

EPO-464

Epidemiological characteristics of pediatric multiple sclerosis in Republic of Tatarstan for 2015- 2019 years

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Background and aims: Aim: to specify epidemiological characteristics of pediatric multiple sclerosis in Republic of Tatarstan.
Methods: Materials and methods: a retrospective analysis of the register of MS patients from 2015 to 2019 years was conducted. The sample included 2,351 patients.
Results: Results and discussion: In 2015, 11 children with MS were observed with annual prevalence rate of 1,4/100,000; the number of new cases-6, the incidence amounted to 0,8 /100,000 per year. In 2016 – 10 patients with annual prevalence rate of 1,2/100,000; new cases-5; the incidence was 0,6/100,000. eight pediatric MS in 2017 with annual prevalence rate of 1,0/100,000, also four new cases with debut were registered. The annual incidence- 0,5/100,000. In 2018 – new nine cases, the annual incidence- 1,1/100,000. The total number of the patients was 13 with annual prevalence rate of 1,6/100,000; In 2019 the number of confirmed pediatric MS cases amounted 11 children, the annual prevalence rate of 1,3/100,000; new cases were reported in two patients with annual incidence- 0,2/100,000 per year. The age of MS debut: the disease most often began in the period from 18 to 30 and from 30 to 40 years (40,4–50,3% and 25,8–29,3% respectively), however 10% of cases were under the age of 18 years. Expected incidence of pediatric MS in RT in 2019 should have been at least 1,9/100,000 per year, but actually amounted to 0,2/100,000.
Conclusion: This study revealed low prevalence and incidence of pediatric MS (1–1,6 per 100,000) and (0,2–1,1 per 100,000 per year).
Disclosure: Study group have no relevant conflicts of interest to declare.

Muscle and neuromuscular junction disease 3

EPO-465

Very late-onset Myasthenia gravis

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Background and aims: Very late-onset myasthenia gravis (VLOMG) is defined as MG with onset above 65 years-old. Several studies have reported an increasing incidence of VLOMG. The main goal was to perform a retrospective analysis of patients with VLOMG.
Methods: Among the 217 MG patients followed in our Neuroimmunology Outpatient Clinics we identified those with VLOMG between 2008–2020 and data was retrospectively collected.
Results: We identified 36 patients (16,5%), 21 (58.3%) were males. The age of onset ranged between 65 and 86 years (M=72.53; SD=5.35). Classification of the disease at presentation was I (n=13;36.1%), II (n=3;8.3%), IIA (n=7;19.4%), IIB (n=10;27, 8%), IIIB (n=2;5.6%) and V (n=1; 2.8%). The disease was generalized in about 80% of patients. Ocular myasthenia was present in seven (19.4%). Repetitive stimulation on EMG was positive in 27 (75.0%). Anti-RAch antibodies were positive in 30 (83.3%), four (11.1%) double seronegative and two (5.6%) negative for anti-Rach and not tested for anti-MuSK. Anti-titin antibody was found in nine (25.0%), and from those two had thymoma. Three (8.3%) underwent thymectomy for removal of thymoma. Almost all patients underwent treatment (n=35;97.2%): pyridostigmine-33 (91.7%), oral steroids-28 (77.8%), and immunosuppression-19 (52.8%). From the latter: 14 (73.7%) azathioprine, three (15.8%) methotrexate and two (10.5%) MMF. IVIg was administered in 11(30.6%) patients. Two (5.6%) required invasive ventilation. About half (53.5%) of the patients are in pharmacological remission.
Conclusion: As reported in the literature, ocular presentation was the commonest manifestation. Therapeutic response was very good in about half of patients, however 52.8% needed long-term immunosuppressive therapy.
Disclosure: Nothing to disclose.

EPO-466

Rituximab treatment in myasthenia gravis: a serie of eight patients

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Background and aims: Myasthenia gravis is an autoimmune disorder of neuromuscular junction. Traditionally, long-term treatment of myasthenia gravis has been performed with corticosteroids and other immunosuppressants. Some patients present a refractory myasthenia gravis despite immunosupressant treatment. As an anti-CD20 monoclonal immunoglobulin, Rituximab has shown some evidence of benefit in patients with myasthenia.
Methods: Retrospective descriptive analysis of medical records of eight patients of our department with diagnosis of myasthenia gravis treated with Rituximab.
Results: All patients were women, with a median age at onset of 69,45 years old. seven patients had a generalised form of myasthenia gravis. 100% of patients showed positive anti-Ach receptor antibodies. All of them had been treated with others immunosuppressants prior to Rituximab. In two out of eight patients thymoma was diagnosed. Six patients underwent thymectomy during the course of the disease. Median time from diagnosis to Rituximab was 12,3 years. four patients received 375 mg/m2 weekly, and three received 500mg-1gr/15 days. Six patients remained stable after Rituximab treatment. One patient presented an important clinical improvement. In one of the patients, clinical course of the disease remained refractory.
Conclusion: Rituximab shows good results in treatment of patients with refractory myasthenia gravis, which has been widely described on literature before. In our cohort, time from diagnosis to treatment with rituximab was quite long, and data related to long-term treatment with Rituximab is scarce in some cases. Clinical improvement must be assessed after long term treatment, and through clinical and quality of life scales.
Disclosure: No disclosure.

EPO-467

Immune-Mediated Necrotizing Myopathy – A case-report

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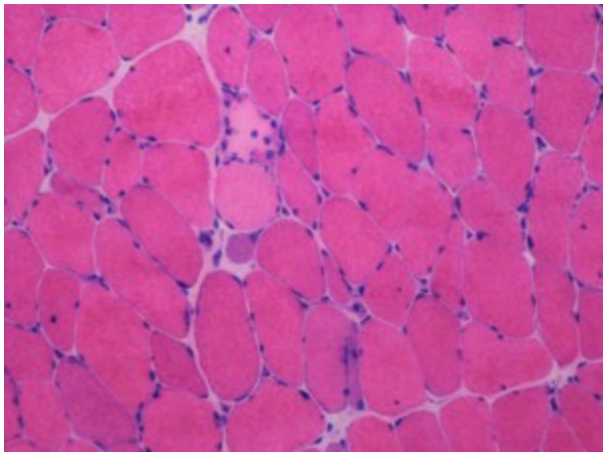
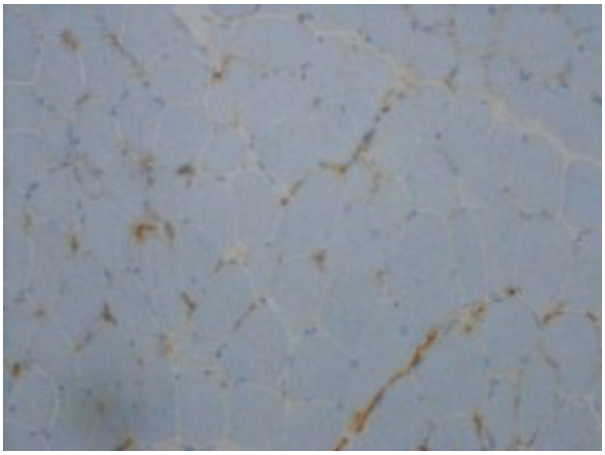
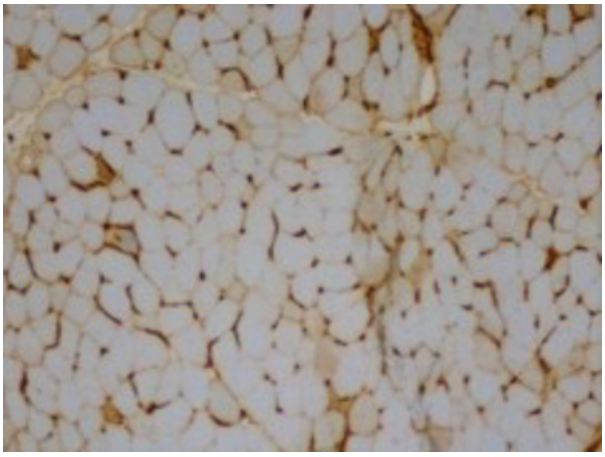
Background and aims: Inflammatory myopathies are a heterogeneous group of rare autoimmune diseases characterized by muscle weakness, muscle enzymes elevation, presence of autoantibodies and inflammatory pattern in muscle biopsy. Immune-Mediated Necrotizing Myopathy (IMNM) represents 20-30% of cases and average age of onset is between 40 and 60 years. It is distinguished from other inflammatory myopathies by the existence of muscle fiber necrosis associated with low inflammatory infiltrate. It has an important association with tumors and, in some cases, there is a previous history of statin exposure. Two autoantibodies associated with IMNM have been described: anti-SRP (Signal Recognition Particle) and anti-HMGCR (3-hydroxy-3-methyl-glutaryl-CoA reductase), but studies to assess their role in disease pathogenesis is still under progress.
Methods: Not-applicable.
Results: 62-year-old man, with three months evolution of progressive muscle weakness, proximal predominance, beginning at lower limbs, progressing to upper limbs, myopathic gait, dysphagia, asthenia and weight loss. Complementary study was suggestive of muscular pathology. Infections, toxic and systemic diseases were excluded. Muscle biopsy was crucial for IMNM definitive diagnosis. Anti-SRP and anti-HMGCR antibodies were negative. To rule out an occult tumor, the patient performed 18F-FDG-corporal-PET, upper gastrointestina endoscopy, thoracoabdominal-CT and no changes were found. The patient started prednisolone 60mg daily and mycophenolate mofetil 1000mg twice-daily, with progressive improvement of weakness and dysphagia. He maintains follow-up consultations and is subject of study for a possible neoplasia.



Anatomopathological study of the muscle (Hematoxylin-eosin stain)



Anatomopathological study of the muscle - Immunohistochemical analysis of C3 and C9 (C5b-9) staining(C5b-9)



Anatomopathological study of the muscle (MHC-1 stain)

Conclusion: Although rare, IMNM is a diagnosis to be considered in the presence of a suggestive clinical presentation, given the possibility of associated concomitant pathologies and patient improvement with early treatment initiation.
Disclosure: Authors have no conflict of interest to declare.

EPO-468

Hereditary Myopathy with Early Respiratory Failure with Neurogenic Features on Electrophysiology and Muscle Biopsy

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Background and aims: Hereditary Myopathy with Early Respiratory Failure (HMERF) is a slowly progressive myopathy, typically presenting in mid-adulthood with distal leg weakness and evidence of respiratory muscle weakness, with or without respiratory symptoms.
Methods: A patient with clinical lower motor neuropathy and positive family history for muscle disease was investigated in the motor neurone disease clinic with standard electrophysiological testing and genetics testing. The clinical picture was further clarified with muscle biopsy, and MRI of both the neural axis and thigh muscles.
Results: Genetics testing showed that he was heterozygous for the c.95134T>C p.(Cys31712Arg) pathogenic variant in the TTN gene. Electrophysiological testing showed widespread denervation consistent with anterior horn cell disease. Muscle biopsy confirmed the existence of both known titinopathy changes and neurogenic changes. MRI showed cervical stenosis and mild cord signal change with no clinical correlation, and also fatty infiltration of the thigh muscles consistent with HMERF.
Conclusion: HMERF can mimic a lower motor neuropathy and show electrophysiological features consistent with anterior horn cell disease. Diagnostic uncertainty should be followed up with other investigations such as muscle biopsy and MRI.
Disclosure: Nothing to disclose.

EPO-469

Myasthenia gravis in Poland- healthcare burden in nationwide cohort

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Background and aims: Myasthenia gravis (MG) is a rare autoimmune disorder of neuromuscular junction. MG healthcare burden has not been studied in Poland before.
Methods: Data was drawn from the National Health Fund database; MG patient was defined as a person who received at least once medical service coded with ICD-10 code MG (G70) and at least two reimbursed prescriptions for pyridostigmine bromide or ambenonium chloride in two consecutive years. We have analyzed treatment: chronic immunosuppression, intravenous immunoglobulins (IVIg), plasma exchange (PE), number, length of hospitalizations, intensive care unit (ICU) care and deaths between 2013–2018.
Results: In 2018, there were 9012 MG patients (F:M 1.62:1), 30.6% had early onset MG (<50 years). 66.3% received symptomatic treatment only, 33.7% – glucocorticoids (GCS) and/or other immunosuppressants (IS) – (64.6% GCS only, 17.5% – azathioprine plus GCS, 11% – azathioprine only, 4.6% – GCS plus other IS (methotrexate, mycophenolate mofetil, cyclosporine or tacrolimus), 2% – other IS only. In 2018, 42.3% of patients were hospitalized at least once (mean 2.05 per year), 13.7% due to MG (1.47 per year). In 2018, 1.63% of MG patients received PE, 2.33% IVIg. In 2013–2018 0.8–1.0% of MG patients/year were hospitalized in ICU with average length of stay 10.8–14.0 days/patient, 2.08% of MG patients in 2018 had myasthenic crisis. Mean age at death was 75.7 years for MG, and 73.9 for general population (p=0.006). All-cause mortality was higher for men (4.1–5.1%) than for women (2.5–3.1%).
Conclusion: Our findings confirm significant healthcare burden of MG, comprising a tool to plan resources needed for MG patients.
Disclosure: Authors declare no conflict of interest and no financial support to disclose.

EPO-470

Pembrolizumab-induced neuromuscular overlap syndrome

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Background and aims: Pembrolizumab is an immune checkpoint inhibitor (ICI) with good results against metastatic melanoma, but with inflammatory side effects related to immune activity. Although rare, neuromuscular disorders represent the most common neurological ICI-induced toxicity.
Methods: N/A
Results: A 76-year-old man with metastatic melanoma presented with binocular diplopia, four weeks after the first treatment with Pembrolizumab. Neurological exam suggested a right 4th nerve palsy. Head-CT was unremarkable. One week after, it progressed to complex ophthalmoparesis, a right fatigable ptosis and dropped head. Laboratory testing revealed high levels of serum creatine kinase (12.632 U/L). Oral prednisolone and pyridostigmine was started. On the next day he presented a worsened complex ophthalmoparesis, dysphonia and excessive sweating. Limb muscle strength and deep tendon reflexes (DTR) were preserved. The results for nerve conduction study, high frequency repetitive stimulation and single fibre electromyography were negative. The patient then developed severe respiratory failure and became dependent on continuous positive airway pressure ventilation. Neurological deficits also progressed to proximal tetraparesis and DTR abolition. CSF analysis showed mild protein elevation. Intravenous human immunoglobulin was started, without clinical improvement. Further diagnostic workup with brain-MRI and anti-neuronal antibodies were normal. A second EMG revealed generalized fibrillation potentials and positive sharp waves, even on diaphragm. Rescue treatment with plasmapheresis was attempted but patient died after the first session.
Conclusion: This case describes a neuromuscular syndrome with coexisting clinical features of Miastenia Gravis and myositis. ICI neurotoxicity can present as overlapping neuromuscular syndromes, making diagnosis challenging.
Disclosure: Nothing to disclose.

EPO-471

Statins and asymptomatic hyperCPKemia: should we look for anti-HMGCR antibodies more frequently? A case report

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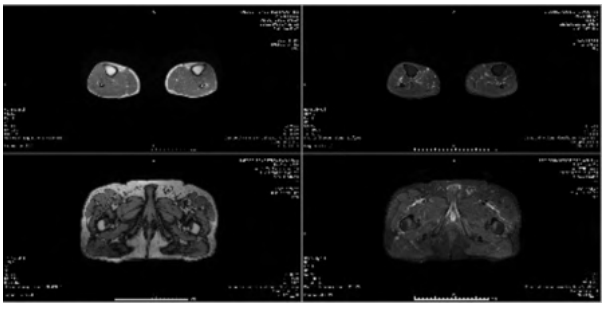
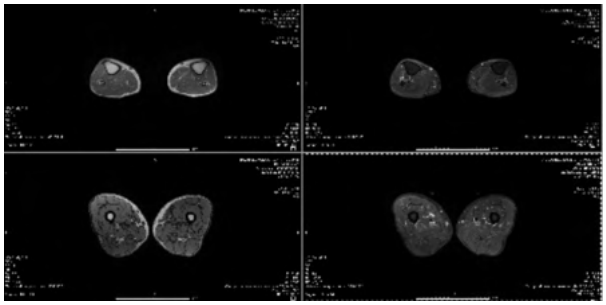
Background and aims: Statin-related myositis usually presents with bioptical necrotizing features (necrosis, low presence of lymphocytes, macrophagic infiltrates), CPK increase, inflammatory muscle MRI features. Patients tend to suffer from predominant proximal weakness. Treatment is recommended and is based on immunosuppressive or immunomodulatory therapies (steroids, IGs, rituximab, other immunosuppressants). We present the case of an asymptomatic, 72 years old patient, that has been undergoing several diagnostic procedures since 2018, when hyperCKemia was discovered. He had been taking statins since two years before and then discontinuated them. Since 2018, his CK levels were permanently high but he was clinically negative at neurological examination at follow-up visits.
Methods: The patient underwent muscle biopsy, muscle MRI, seriate CPK dosage, DNA testing for LGMDs, myositis-related antibodies dosage including anti-HMGCR.
Results: Muscle biopsy showed minimal myopathic changes with positive HLA finding. Muscle MRI of the pelvis and inferior limbs showed minimal inflammatory changes in the legs. CK levels were always under 1,500 U/L. DNA analysis tested negative. Myositis associated antibodies proved negative, but anti-HMGCR resulted increased.



STIR and T1 seq. of our patient's muscle MRI, showing absence of oedema or adipose tissue infiltration.



STIR and T1 seq. of our patient's muscle MRI, showing absence of oedema or adipose tissue infiltration.

Conclusion: Based on laboratory and MRI findings, and the history of previous statins medication, the patient was diagnosed with statin-related IMNM. A small number of LGMD-like antiHMGCR myositis cases have been described, but to our knowledge no other cases of persistently asymptomatic patients have been reported. The clinical stability and negativity at neurological examination makes us question therapeutic management, while suggesting the opportunity of antiHMGCR testing in a-paucisymtpomatic patients with history of statin medication use and hyperCPKemia.
Disclosure: Nothing to disclose.

EPO-472

Unexpected but successful non-instrumental vaginal delivery in a spinal muscular atrophy type II pregnant patient

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Background and aims: Spinal muscular atrophy (SMA) is an autosomal recessive motor neuron disorder caused by homozygous deletion or mutation in 5q11.2-q13.3, affecting the SMN1 gene. It is characterized by progressive lower motor neuron loss in the brainstem and spinal cord, resulting in muscle weakness and atrophy.
Methods: A case report of a non-instrumental vaginal delivery in a patient with SMA type II.
Results: We present a 35-year-old nullipara with SMA type II diagnosed at the age of 14 months. Motor milestones have been delayed since the age of 12 month, with severe muscle weakness of both upper and lower limbs. She retained the ability to sit since the age of 12 months, but she was never able to walk. She had a spinal scoliosis surgery and tracheotomy after a severe pneumonia, becoming dependent on invasive ventilation since then. At the age of 35 years, she became pregnant for the first time and was considered at high-risk, and followed closely by a multidisciplinary team. At 32 weeks, she gave unexpectedly birth at home, without complications and any help of health professionals.
Conclusion: Preterm labour is much more common in mothers with SMA than in general population, especially in SMA type II, and the need for instrumental (vacuum extraction or forceps) or caesarean delivery is drastically increased. Our case is the first one reporting a non-instrumental vaginal delivery in a patient with SMA type II (pregnancy outcomes in all previously reported SMA type II women are summarized in table 1).

Case Report	Preterm labour (weeks)	Instrumental delivery	Caesarean
Yau et al (3)	+ (34)		+
Carter et al (4) Case 1	-	Vacuum	
Carter et al (4) Case 2	-		+
Pugh et al (5)	+ (33)		+
Plaut et al (6) Case 1	+ (28)		+
Case 2	+ (28)		+
Harris et al (7)	+ (34)		+
Macnaill et al (8)	+ (31)		+
Habib et al (9)	+ (36)		+
Bollag et al (10)	-		+
Coffman et al (11)	+ (36)		+
Rudolik-Schonehorn et al (12)	+ (34)		+

Pregnancy outcomes in women with SMA type II

Disclosure: Nothing to disclose.

EPO-473

A juvenile case of Lambert-Eaton myasthenic syndrome resembling a congenital Myasthenic Syndrome

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Background and aims: Lambert-Eaton myasthenic syndrome (LEMS) is an autoimmune disorder of the presynaptic neuromuscular junction, resembling presynaptic Congenital Myasthenic Syndromes (CMS), sharing the same electrophysiological features and clinical signs. Unlike CMS, LEMS is rare in children and young adults, with only 12 cases reported in the literature.
Methods: We report a juvenile case of LEMS with proximal weakness, areflexia, positive serum P/Q-type voltage-gated calcium channel antibodies (VGCC) and the characteristic increment in compound motor action potential (CMAP) on high-frequency repetitive nerve stimulation.
Results: An 18-year-old female patient, presented at age of 16 with muscle fatigue, walking disability, frequent falls and difficulty in climbing stairs. Her past history is marked by congenital strabismus, kidney malformation and a Wolff-Parkinson-White syndrome. Neurological evaluation disclosed mild ptosis, myopathic gait, mild axial and proximal muscle weakness with slight fatigability and abolished reflexes. Neurophysiological evaluation showed a reduced CMAP amplitude, a decrementing CMAP response to low-frequency repetitive nerve stimulation (35%) with an increment following maximum voluntary muscle contraction during 2min (100%). Needle EMG revealed a slight myopathic pattern. Blood analysis disclosed a VGCCs antibodies of 299,7 U/mL (reference value <40). A neoplastic condition was ruled out. Initial treatment with pyridostigmine and intravenous immunoglobulin (IVIg) showed partial improvement, and she is now stabilized with amifampridine.
Conclusion: Our case illustrates a juvenile case of primary autoimmune LEMS. Unlike adults, non-paraneoplastic LEMS prevailed in children but close surveillance for development of cancer for at least two years should be performed.
Disclosure: Nothing to disclose.

EPO-474

Enzyme replacement therapy in late-onset Pompe disease patients: an experience of a Portuguese universitary hospital

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Background and aims: Pompe disease (PD) is a rare lysosomal storage disorder caused by deficiency in acid alpha-glucosidase (GAA) resulting from mutations in the GAA gene in chromosome 17. Late-onset PD (LOPD) is characterized by progressive limb-girdle muscle weakness, muscle atrophy, respiratory failure and hyperCKemia. In 2006 recombinant human alglucosidase alfa was approved as enzyme replacement therapy (ERT) for all forms of PD.
Methods: Retrospective and descriptive analysis of six patients with LOPD treated with ERT, through screening of medical records from January 2008 until September 2020. Motor scales (Medical research Council, Gait-Stair-Gowers-Chair Score, 6-minute walking test) and respiratory function tests (forced vital capacity, maximal inspiratory and expiratory pressures) were used to monitor treatment effectiveness.
Results: We included six LOPD patients with overt muscle weakness, being four female (66.6%) with a mean age of 56.5±15.3 years (36-77). Mean onset age was 29.5±3.6 years (20–56) and mean onset treatment age was 48.1±16,8 years (23–69). Maximal treatment duration was 13 years (mean 8.3±3.7). After three years of treatment, a cross-sectional study was carried out, finding that all patients remained stable in relation to muscle strength (mean pre-treatment 75.2±13.3; post-treatment 74±12.3), functional outcome (mean pre-treatment 24.2±6.3; post-treatment 21.7±6.3) and respiratory function (mean forced vital capacity pre-treatment 2.6±0.7; post-treatment 2.6±0.7).
Conclusion: Our results were consistent with previous studies reported in the literature, in which the majority of patients under ERT remained stable or slightly improved their condition, especially in the first years of treatment.
Disclosure: Nothing to disclose.

EPO-475

Asymmetrical limb myopathy as a new phenotype of CASQ1 myopathy

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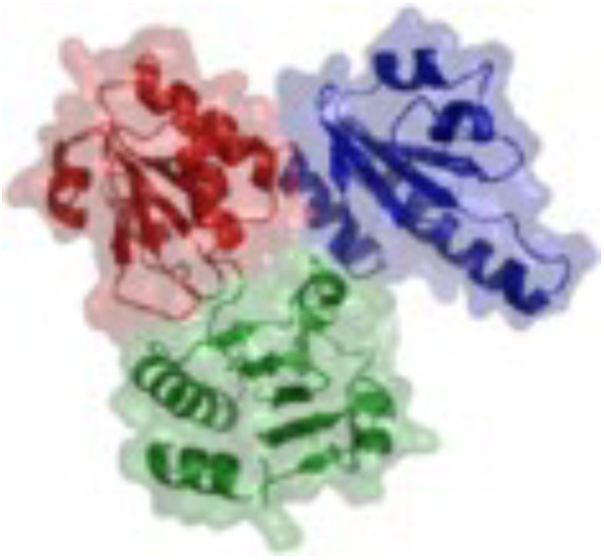
Background and aims: CASQ1 myopathy is a rare disorder with variable phenotype.We diagnosed a family with high CK ,inherited club-foot the index case an 11 year-old girl presented weakness and asymmetry of R lower limb.
Methods: Ca2+ ions are crucial in skeletal muscle excitation- contraction coupling. Synchronous Ca2+ release from the sarcoplasmic reticulum (SR) terminal cisternae (TC) into the cytoplasm and its reuptake in SR are granted by a structural and functional unit of Ca2+ sensors, release channels, buffering proteins, and ATP-dependent Ca2+ pumps at the junction of T tubule and the triad.. Diseases involving the triad have been identified and calsequestrin mutation is a rare cause of this dysfunction. By NGS search CASQ1 mutation was identified in the index case.



Calsequestrin a storage protein of SR

Results: The index patient showed degenerating single fibers and scattered regenerating fibers in biopsy EMG showed both myogenic and neurogenic changes, The girl was operated at 14 years for right femur elongation and left femur epiphyseolysis but remained weak.
Conclusion: Because of a paucity of symptoms, it is likely that CASQ1 mutations may remain undiagnosed in the index case a muscle biopsy was performed, however unspecific myopathy was found, only detailed molecular studies allowed identification.
Disclosure: Telethon and eurobiobank.

EPO-476

Refractory myasthenic crisis in a patient with refractory Myasthenia gravis and COVID-19

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Background and aims: Myasthenia gravis (MG) is an autoimmune, antibody-mediated disease of the neuromuscular junction causing muscle weakness. Due to immunosuppression and possible respiratory/bulbar muscle weakness, MG patients are at risk for developing severe coronavirus disease 2019 (COVID-19).
Methods: Case report.
Results: A 62years old patient suffered from bulbar onset generalized MG with acetylcholine receptor antibodies since eight months. He survived two prior MC and was nourished via percutaneous enterogastrostomy (PEG) despite symptomatic treatment and immunosuppression with azathioprine and steroids (severity graded according Myasthenia gravis foundation of America score (MGFA) IVb). He presented with fever, cough and severe generalised muscle weakness. Polymerase chain reaction confirmed COVID-19, ventilatory failure prompted mechanical ventilation (MV). Intravenous immunoglobulins (ivIg) and pyridostigmine i.v. were given. Weaning had to be postponed because of respiratory muscle weakness and septicaemia with Enterobacter cloacae, treated with appriopriate antibiotics. Not until removal of PEG sepsis resolved and plasmapheresis (PLEX) was conducted. The patient reached spontaneous breathing via tracheostomy, but still needed nasogastric tube feeding (MGFA V). Because of missing further progress of bulbar muscle function complement inhibition with eculizumab was administered (900mg 1 x weekly for four weeks, thereafter 1200mg every two weeks). After the second dose tracheostomy and nasogastric tubes could be removed, bulbar and generalized weakness resolved on follow-up (MGFA IIa).
Conclusion: Our patient experienced MC triggered by COVID-19 and suffered from prolonged sepsis. After failure of standard treatments (IvIg/PLX) eculizumab was given, followed by marked recovery. The role of complement inhibition for treatment of refractory myasthenic crises should be further studied.
Disclosure: Ulrich Hofstadt-van Oy reports speaker honoraria from Alexion and Hormosan, the other authors have nothing to disclose.

EPO-477

Late-onset axial and limb-girdle myopathy with early respiratory failure due to novel mutations in the SEPN1 gene

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Background and aims: SEPN1-associated myopathies are rare congenital myopathies which may manifest in childhood or adolescense. Several phenotypes have been described: (a) Rigid-spine myopathy; (b) Mallory body-like myopathy; (c) Multi-minicore myopathy; (d) congenital fibre type disproportion. All adult cases described so far, showed clinical symptoms before the age of 15, and survival up to the 6th decade is rare.
Methods: A 60-year old patient developed slowly progressive axial and limb girdle weakness, muscle pain and spinal rigidity starting at the age of 50. Respiratory failure due to respiratory muscle weakness emerged whilst the patient was still ambulant. Further laboratory, biopsy, MR-imaging and molecular genetic work-up was performed.
Results: Laboratory testing revealed haematological abnormalities: macrocytosis, anisocytosis of the platelets, granulocytosis and lymphopenia. CK was only mildly elevated. Muscle biopsy only showed some non-specific changes with normal ultrastructure of the sarcomeres and mitochondria. Molecular genetic analysis demonstrated two compound heterozygous missense mutations (p.Leu331Pro and p.Ala440Thr) in the selenon gene which have not been described before. Using muscle MRI as a biomarker, these mutations were eventually classified as pathogenic.
Conclusion: Disease onset at the age of 50 is the latest described so far and thus further expands the phenotypic spectrum of SEPN1 deficiency. The haematological abnormalities observed in the patient partly resemble those seen in acquired selenium deficiency; however, plasma selenium levels were within normal range and substitution of selenium did not improve the clinical symptoms nor did it correct the abnormalities of the blood count.
Disclosure: Nothing to disclose.

Neuroimaging 2

EPO-478

Microstructural and functional cerebral alterations in idiopathic generalized epilepsy

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Background and aims: Idiopathic generalized epilepsy (IGE) is an umbrella term for a group of epileptic disorders of numerous phenotypes afflicting paediatric patients without crude abnormities in clinical brain imaging and generally normal intelligence, albeit with minor behavioural alterations.
Methods: In the search for possible structural or functional cerebral correlates of IGE and the neuropsychological signature, the presented pilot study compared nine IGE patients (ages 14–16, 6 females) and nine healthy controls (ages 13–17, two females) utilizing a complex neuropsychological test battery and a multimodal MRI protocol including structural scans, diffusion weighted imaging and resting-state functional MRI acquired at a 3T Siemens Prisma Scanner.
Results: While no differences were found in the cortical thickness, IGE patients had lower mean diffusivity in the bilateral cingulate and motor cortex ($p<0.05$, within modality FDR correction). The amplitude of low-frequency fluctuations in the resting state functional MRI was also significantly lower over large prefrontal and parietal cortical areas, brainstem and bilateral striatum ($p<0.05$, within modality FDR correction). Other parameters of interest as fractional anisotropy and degree centrality failed to reveal any substantial inter-group differences. On the other hand, neuropsychology testing detected significantly lower full scale intelligence quotient in the IGE group, with predominant affection of verbal and verbal comprehension indices. No inter-group differences were found in anxiety and depression scales.
Conclusion: These preliminary data point to considerable IGE-related brain alterations, be it on the microstructural or functional scale, combined with mildly, but still significantly lower intelligence. While far from final, our conclusions definitely warrant continued research.
Disclosure: Nothing to disclose.

EPO-479

Identification of epileptic foci in refractory epilepsy through functional and structural connectivity based on MRI

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Background and aims: Epilepsy is considered a disease in which ictal/interictal activity is generated and propagated through neuronal networks. Functional and structural connectivity, which can be implemented through magnetic resonance imaging (MRI), provide information about the network nature of epilepsy. With tractography and resting-state functional MRI (rs-fMRI), we aim to improve the identification of epileptic foci through connectivity analyses.
Methods: This prospective study was approved by the Institutional Review Board. The study comprised 10 patients (3 women, seven men; mean age: 31±10 years; range: 21–50 years). The selection criteria were adults with drug-resistant epilepsy, undergoing a clinically indicated standard MRI refractory epilepsy protocol, electrocorticography, video-EEG, F18-FDG PET or SPECT with possible treatment by surgery. In addition to the standard protocol, rs-fMRI, tractography and a 3D T1-weighted image (wT1-3D) were acquired and post-processed (Table 1). A Crawford-Howell t-test was implemented to compare structural and functional connectivity matrices of each patient with healthy groups, obtaining contrast matrices (Figure 1). Maps were generated identifying clusters of four or more regions with significant differences (threshold of $p<0.05$), and they were compared with the patient's clinical diagnosis.

	wT1-3D	Tractography	rs-fMRI
Scanning Sequence	GRE	EPI_SE	EPI_GRE
Slice Thickness [mm]	1	3	4
GAP [mm]	0	0	0
Matrix	256x256	80x80	96x96
Echo Time [ms]	3.276	92.7	23
Repetition Time [ms]	7.812	12000	2000
Flip Angle [°]	12	90	90
n	10	4	10
Software toolboxes		FSL Bedpostx, Probtrackx2	CONN*, SPM 12*

Table 1: Summary of sequences design and software toolboxes. *Matlab R2019a.

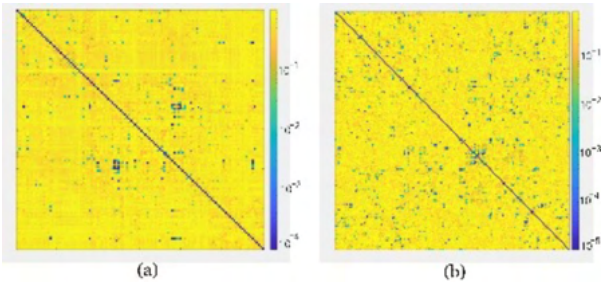

Figure 1: Patient with an epileptic focus in the temporal lobe. (a) Structural connectivity matrix. (b) Functional connectivity matrix.

Results: The most statistically significant areas were visually identified in the contrast maps and compared with post-surgical results. Structural and functional connectivity maps were initially analysed separately, and then simultaneously. Results are shown in Table 2.

	Tractography	rs-fMRI	Tractography +rs-fMRI
TPR (%)	40.0	86.67	100.0
TNR (%)	88.27	73.07	93.45
PPV (%)	17.39	18.84	45.0
NPV (%)	95.97	98.7	100.0

Table 2: Performance to locate epileptic foci. TPR: Sensibility, TNR: Specificity, PPV: Positive Predictive Value, NPV: Negative Predictive Value.

Conclusion: The simultaneous analysis of structural and functional connectivity improves the tractography TPR and the TNR of rs-fMRI. The PPV can be improved by increasing the sample of patients and healthy subjects.
Disclosure: Nothing to disclose.

EPO-480

Spondylodiscitis - is it always just an inflammatory process?

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Background and aims: Spondylodiscitis is an inflammatory disease of the vertebral column and the intervertebral space (spine joints and intervertebral discs). Changes associated with spondylodiscitis in the vast majority of cases are epidural abscesses of the spinal cord and inflammatory abscesses of the paraspinal muscles. The purpose of the work was monitoring spondylodiscitis lesions in magnetic resonance imaging.
Methods: A group of 23 patients, with recognized degenerative spine disease in X-ray and CT scan, was qualified for the research. Due to exacerbation of pain MRI was performed in all patients. Then, in a group of eight patients, a follow-up MRI was ordered in the period of 8–12 weeks due to persistence of clinical symptoms despite implemented treatment.
Results: Spondylodiscitis lesions were found in all patients during the MR examination. Additionally, in 14 patients coexistence of epidural abscess was diagnosed, of which nine patients had signs of subsequent spinal stenosis. Moreover, in 12 patients, inflammatory changes were found in the soft tissues of the back and the perivertebral column. In three patients clearly enlarged, reactive lymph nodes were visualized. In a control MRI, two patients were diagnosed with disseminated neoplastic process against the background of partial regression of inflammatory changes. The remaining patients in this study showed regression of the inflammatory lesions.
Conclusion: Extensive spondylodiscitis lesions may obscure the underlying neoplastic process. In the setting of persistent pain in patients with spondylodiscitis, a follow-up magnetic resonance imaging is recommended not only to assess the regression of inflammatory lesions, but also to evaluate for possible concomitant pathologies.
Disclosure: Nothing to disclose.

EPO-481

Stroke-like migraine attaks after radiation therapy: a rare complication

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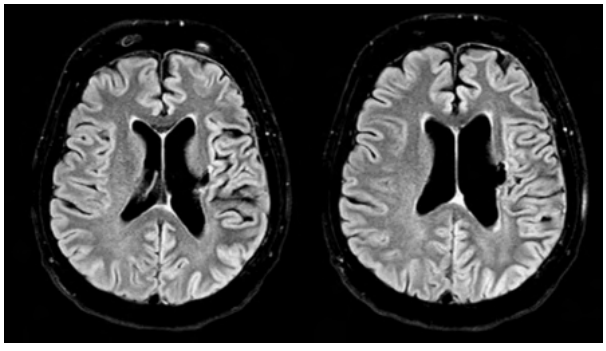
Background and aims: Stroke-Like Migraine Attacks After Radiation Therapy (SMART syndrome) is a complication related to radiotherapy. It is characterized by focal neurological deficits (aphasia, hemiplegia, hemianopia), migraine-like headaches and seizures. The diagnosis is clinical and radiological. Magnetic resonance imaging (MRI) shows unilateral cortical gyral thickening and enhancement, predominantly in temporal-parieto-occipital areas in FLAIR and T2 sequences. Most cases have a complete recovery without treatment, but the use of corticosteroids to speed up recovery has been described.
Methods: Clinical and radiological description of a patient treated in our centre for neurological deterioration, seizures and headache. Literature review of SMART syndrome.
Results: A 40-year-old patient with a history of left frontal-parietal anaplastic astrocytoma treated with radiotherapy in 2009 and with a consequence of motor aphasia and mild right hemiparesis, consulted to our centre for worsening of aphasia, right hemiplegia and for the appearance of headache and right homonymous hemianopia. During the admission he presented a generalized seizure. Blood tests and cerebrospinal fluid studies were performed with no pathological findings. Serial electroencephalograms showed signs of left hemispheric dysfunction without epileptiform graph elements. The study was completed with a MRI that showed a left cortical thickening and hypersignal in FLAIR associated with left frontal-parieto-temporal-occipital-insular gyral enhancement. Treatment with prednisone was started with a good clinical response.



MRI: left cortical thickening and hypersignal in FLAIR associated with left frontal-parieto-temporal-occipital-insular gyral enhancement.

Conclusion: SMART syndrome should be considered in those patients with a history of brain radiation therapy who present subacute neurological deficits with a compatible MRI. Corticosteroids can improve the symptoms, although their use remains unclear.
Disclosure: Nothing to disclose

EPO-482

Resting-state networks in a fully conscious hemispherectomized patient

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Background and aims: Functional MRI (fMRI) resting-state (rs) networks (RSNs) – especially the default mode network (DMN) – is considered essential in preserved consciousness. Recent rs-fMRI findings show decreased DMN connectivity in patients with brain-damage and impaired consciousness. However, changes in brain morphology due to structural brain-damage complicates the analysis and interpretation of RSNs, risking erroneous classification of consciousness level. Here, we investigated RSNs in a hemispherectomized, but fully conscious patient compared to healthy controls (HC).
Methods: A 45-year-old man, who six years previously suffered from a malignant middle cerebral artery infarction and atrophy of the right hemisphere, was clinically evaluated with neuropsychological testing and scanned with rs-fMRI. Mean within-network connectivity estimates for eight canonical RSNs (default mode, sensorimotor, visual, salience, dorsal attention, frontoparietal, language and cerebellar network) were extracted and compared to 20 HCs scanned under the same conditions. Differences in connectivity were computed as z-scored standardized to HCs. Patient data were analyzed with and without accounting for structural brain-pathology.
Results: Compared to HCs, the patient showed decreased connectivity in all RSNs with z-scores ranging from -4.56 (salience network) to -1.83 (cerebellar network) and -2.15 for the DMN. We anticipate normal or perhaps increased connectivity in the patient in specific network edges between preserved brain areas.
Conclusion: A conscious hemispherectomized patient showed abnormal rs-network connectivity when fMRI-analysis was performed without accounting for brain-pathology. We anticipate this abnormality is confined to damaged brain areas, underscoring that region-specific brain integrity is critical when using fMRI to estimate consciousness level. Full data will be presented at the congress.
Disclosure: Authors declare no conflicts of interest.

EPO-483

Brain volumes alterations in multiple sclerosis patients: comparison to QyScore® normative data

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Background and aims: Whole-brain (WB), Grey (GM) and White Matter (WM) atrophy have been suggested as surrogate markers of neuroaxonal loss and disease progression in Multiple Sclerosis (MS). We aim at assessing Magnetic Resonance Imaging (MRI) differences in brain structures volumes between relapsing-remitting MS (RRMS) and healthy controls (HC) , and compare them to a large-scale normative database of HC.
Methods: MRI of 27 RRMS patients (40.3±7.3 and F/M=19/8) and 29 age- and gender- matched HC (41.6±11.4 and F/M=19/10) from independent datasets (REACTIV, KIRBY21, OASIS1) were considered. The normative database was composed of 1,292 HC with ages ranging from 20 to 90 years old and 54% of women. WB, WM, GM volumes were processed using QyScore®, an automatic tool for the measurement of brain structures volumes, as well as z-scores obtained from the comparison of brain volumes of each subject against age-matched volumes in the normative database. Group differences were evaluated with a 2-tailed t-test.
Results: Average WB, WM and GM z-scores in the RRMS group were significantly smaller than the HC group (WB z-score (RRMS/HC) =-1.67/-0.34*, WM z-score (RRMS/HC)=-2.00/-1.03*, GM z-score (RRMS/HC)=-0.79/0.22*, *p<0.05).
Conclusion: The comparisons to normative reference data, provided through QyScore®, are in line with previously reported results on RRMS patients. The use of QyScore® normative database for the interpretation of brain volumetric analysis can highly improve the clinical assessment of RRMS patients in clinical routine.
Disclosure: Acknowledgements: Dr Delphine Lamargue-Hamel, PI of the REACTIV study, Dr Mathilde Deloire, research clinical coordinator of the REACTIV study, Pr Aurélie Ruet, team leader of the REACTIV study.

EPO-484

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Artificial intelligence based segmentation of brain structures in MRI. “MRImmuno” study

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Background and aims: A volumetric analysis of specific structures of the central nervous system (CNS) plays an increasingly important role in the monitoring of clinical course and the treatment response in diseases associated with neurodegenerative processes. However, due to the complex anatomic conditions, gathering and analysis of all the necessary imaging data represent very difficult and time consuming processes. Thus the volumetric CNS analysis has been mostly avoided in the current everyday clinical practice.
Methods: “MRImmuno” is an R&D project directed on the development of new digital technologies facilitating the differential diagnostics and therapy monitoring in demyelinating CNS diseases. As a part of the project, a new CNS segmentation algorithm using artificial intelligence “AI” was designed based on the volumetric MRI scans, mainly with the use of T1 sequences. The results generated by the new algorithm were compared with the parameters obtained with the commonly accepted segmentation algorithm. The verification process of both digital tools encompassed the comparison of segmentation accuracy of 100 MRI images. The results were “manually” corrected by two independent radiologists, blinded to the source of segmentation. The accuracy of segmentation was defined based on Jaccard or/and Dice coefficients applied to regions corrected by the researchers and regions generated by assessed algorithms.
Results: At the present level of development, the „MRImmuno” segmentation algorithm proved to be equally accurate with significantly reduced processing time as compared to the commonly accepted segmentation algorithm.
Conclusion: Fast and accurate AI algorithms may facilitate an application of CNS segmentation in everyday clinical practice.
Disclosure: This research was funded by The National Centre for Research and Development grant POIR.04.01.04-00-0118/17.

Neurotraumatology

EPO-487

Epidemiological profile of intracranial trauma in Brazil

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Background and aims: The intracranial trauma is configured as a physical aggression that can lead to anatomical injury in the brain region and is among the most frequent causes of morbidity and mortality worldwide, with an important impact on quality of life.
Methods: This is a descriptive ecological study based on secondary data, obtained from DATASUS. Data were collected regarded the number of hospitalizations and mortality rate due to intracranial trauma in Brazil between the years 2009–2019. They were agrouped by gender and age.
Results: About the analysis of mortality rate and number of hospitalizations, a value of 9.54% and 1,140,150 was found, respectively. In relation to the mortality rate, the highest value was found between people above 80 years old, in both genders. In general, the mortality rate in male group was bigger than in female group, except in children between one and nine years old. The group between 20 and 29 years old had the highest number of hospitalizations, both in men (169,538) and in women (33,929).
Conclusion: This study revealed that despite the hospitalization data decreasing after the age of 20 years, the mortality rate has increased, especially above the age of 40 years. Knowing these data is important to promote a better distribution of resources in order to guarantee equity in care. However, this study has its limitations, and it's necessary to conduct other studies to know more about these findings.
Disclosure: Nothing to disclose.

EPO-488

Features of electroneuromyographic patterns in neuropathies and plexopathies due to gunshot wounds of the extremities

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Background and aims: Gunshot injuries of the peripheral nervous system are a problem of modern neurology, caused by ongoing military conflicts, terrorist attacks. The objective of this study was to identify electroneuromyographic features of post-traumatic gunshot neuropathies and plexopathies.
Methods: We examined 41 men with damage of nerves and plexuses caused by gunshot bullet and shrapnel wounds of the extremities. The average age was 37.5±18.2 years. All patients underwent clinical and neurological examination, stimulation electroneuromyography, ultrasound examination.
Results: As a result of the study, all patients were divided into three groups. In the first group, in 42% of cases of partial damage of the anatomical integrity of the nerve trunk, the action potential of the affected nerve was reduced to 5 ± 3 V. 58% of patients showcased a lack of M-response. In the second group, a low-amplitude polyphase M-response was observed, a significant decrease in the amplitude of the sensory potential of the nerve action was determined to 10±5 V on the lesion side. In the third group, excitation propagation speed along motor fibers in 78% of cases differed from the norm and was within 52±8m/s, while propagation speed along sensitive fibers was 10% lower than normal.
Conclusion: aking into account the peculiarities of electroneuromyographic patterns in case of gunshot injuries of nerves and plexuses contributes to better control of the dynamics of the pathological process, determination of tactics and treatment effectiveness.
Disclosure: This study helps to improve the quality of control of the dynamics of the pathological process and a complex assessment of the effectiveness of therapeutic measures depending on the degree of damage.

EPO-489

The Impact of Social Isolation on the incidence of TBI in Salvador-Ba at the second quarter of last five years

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Background and aims: The COVID-19 pandemic caused radical changes in the daily lives of the population. In this context, actions of social isolation – such as limiting the operation of certain commercial establishments and other actions that prevent the crowding of people – were adopted worldwide to avoid the spread of the SARS-CoV-19 virus. Thus, with the advent of radical changes in the dynamics of society, changes in the pattern of hospitalization in large cities for traumatic brain injury (TBI) can be expected. Therefore, this study aims to trace the epidemiological impact of adopting social isolation on the incidence of TBI in the city of Salvador-Ba, comparing its incidence in the second quarter of the last five years.
Methods: Descriptive observational, cross-sectional study, composed of secondary data published by the Ministry of Health through DATASUS and extracted from the SUS Hospital Information System (SIH/SUS). A period of five years was selected (second quarter of 2016, 2017, 2018, 2019 and 2020) and hospital morbidity data for intracranial trauma, by place of hospitalization, covering the territory of Salvador.
Results: In the second quarter of 2020, 2019, 2018, 2017 and 2016, were registered, respectively: 394, 426, 452, 367, 374 admissions for intracranial trauma in hospitals in Salvador-Bahia.
Conclusion: No significant reduction in the number of hospitalizations during the period of social isolation, compared to previous years. This opposes a perspective that hospitalizations for TBI would reduce in the second quarter of 2020, as a result of installation of the quarantine and risk of contamination in hospitals.
Disclosure: No conflict of interest.

EPO-490

Fainting during blast-related concussion episode increases the chances of persisting headache and insomnia

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Background and aims: Blast-related concussion (BRC) is a form of concussion frequently encountered in soldiers during the war. Post-concussion symptoms (PCS) vary in their duration and intensity after the main episode. Understanding of associated factors impacting the occurrence and maintenance of PCS with time may be of big value in improving the quality of life in war veterans.
Aim: To understand the role of loss of consciousness (LOC) during the BRC episode in later development and number of PCS among veterans of recent Artsakh war.
Methods: Armenian servicemen without severe physical injury who were recovering at a specialized facility were involved in our study. According to the LOC fact at the moment of the blast, they were divided into fainted (FG) and not fainted (NFG) groups. We registered headaches, dizziness, tinnitus/hearing impairment, and insomnia. The number of PCS was counted accordingly.
Results: Of the studied sample, 50% (33) had fainted during BRC episode. Those who fainted had a higher overall number of post-concussion symptoms (2.8 vs 3.45, $p=0.003$). In FG we found a higher number of insomnia (55% vs 45%, $p<0.01$), but not excessive daytime sleepiness (50%, $p>0.05$). Also, participants in FG had more headaches (53.2% vs 46.8%, $p<0.05$). The feeling of dizziness was similar in both groups, while tinnitus was more prevalent in the FG (56.9% vs 43.1%, $p<0.05$).
Conclusion: Our data show that LOC during the BRC episode may be associated with a higher chance of headaches, tinnitus and insomnia but not dizziness in servicemen after war experience.
Disclosure: Nothing to disclose.

EPO-491

Most common in children, but not always

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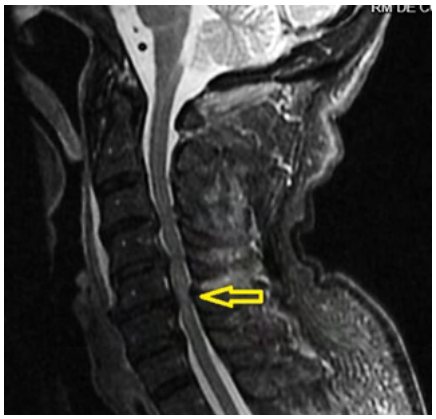
Background and aims: The "Spinal Cord Injury Without Radiographic Abnormality" or SCIWORA is used to name the post-traumatic myelopathy seen in a magnetic resonance with a normal radiography or computed tomography CT. It is more frequent in children younger than eight years due to the biomechanical characteristics of the cervical spine., however it has been also described in adults.
Methods: 86-year-old woman, hypertensive and diabetic, and osteoarticular pathology, that she is brought to the emergency department after accidentally falling from the bed in which she was sitting, falling forward with a mechanism of cervical hyperextension, and head trauma without loss of consciousness.
Results: The evaluation revealed predominantly proximal paraparesis bilateral Babinsky's sign, and left arm paresis, without sensory level. She reported mild diffuse spinal pain, without apophysalgia and without focusing on any region. Data present since the fall. Neurosurgery from another center was contacted for an urgent cervical-dorsal MRI due to the suspicion of post-traumatic acute spinal cord injury. Cervical MRI: degenerative stenosis of the central cervical canal (C3-C4 and C5-C6). Spinal cord injury at C5-C6 without evidence of fracture or understanding. She was finally diagnosed with post-traumatic centromedullary syndrome after a fall in a patient with cervical canal stenosis. SCIWORA of the adult (Spinal Cord Injury Without Radiographic Abnormality).



Cervical magnetic resonance

Conclusion: The patient was admitted with suspected post-traumatic compressive myelopathy. In imaging tests, myelopathy was confirmed, however, no osteoligamentous lesion susceptible to surgical treatment was evidenced. Clinically, the patient evolved to paraplegia, and she was discharged with rehabilitative treatment.
Disclosure: Nothing to disclose.

EPO-492

Analysis of deaths due to traumatic brain injury before and after the implementation of the drunk-driving law in Brazil

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Background and aims: According to the book "Rosen's Emergency Medicine", traumatic brain injury (TBI) describes the craniofacial area trauma caused by external forces. In Brazil, there is a higher incidence of this type of trauma among young people due to automobile accidents. Thus, in 2008, the Brazilian government created the "Lei Seca" (drunk-driving law) to reduce this statistic.
Methods: An ecological study, with data obtained from the SUS Hospitalization System, provided by the Brazilian Ministry of Health through DATASUS. The period was analyzed from May 1998 to July 2018, excluding June 2008, when the law was implemented. This data refers to the group of 20–29 years, considering hospitalizations and deaths TBI related.
Results: There were 167,315 hospitalizations for TBI before the drunk-driving law was implemented, however, after the law was enforced, there was an increase (13.20%). In the ten years preceding the law, the fatality rate was 10.40%, while in the subsequent decade it decreased to 8.62%. The analysis of the death relative risk (RR) showed more vulnerability in relation to TBI compared to other types of trauma, with RR7.01 before the law and RR7.41 afterwards.
Conclusion: An increase in the number of hospitalizations due to TBI was observed in the present study after the application of the "Lei Seca". This may suggest an underreporting of hospitalizations, which impairs the registration of medical records and the credibility of the database. Therefore, it is necessary that public and private companies unite in order to supervise the processing of this information.
Disclosure: Nothing to disclose.

EPO-493

The scenario of traumatic brain injury in Brazil - a cross-sectional study of the last decade

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Background and aims: The traumatic brain injury (TBI) is a disruption or alteration of brain function due to external forces. In trauma, brain injuries are a cause of great concern, due to their poor prognosis and the need for rapid intervention. This study aims to understand the epidemiology of traumatic brain injury in Brazil between 2009 and 2019.
Methods: This is a descriptive study of prevalence. We gathered the data from Brazil's Information System for Notifiable Diseases (SINAN) on deaths from TBI from 2009 to 2019. The odds ratio was calculated (p<0,001) using the EpiInfo software.
Results: In this period, Brazil had 108,748 deaths due to TBI. Throughout the period, there is an average of 9,886 deaths per year, and an annual mortality of 9.54. In relation to the regions, there is higher mortality in the Southeast, 10.47, and lowest in the South, 6.88. Further, we calculated whether the male gender had a higher risk of death, finding an odds ratio of 3,666 (95%CI: 3,611–3,723). The mean time hospitalization was also higher in men (6,5 days) than in women (5,1 days).

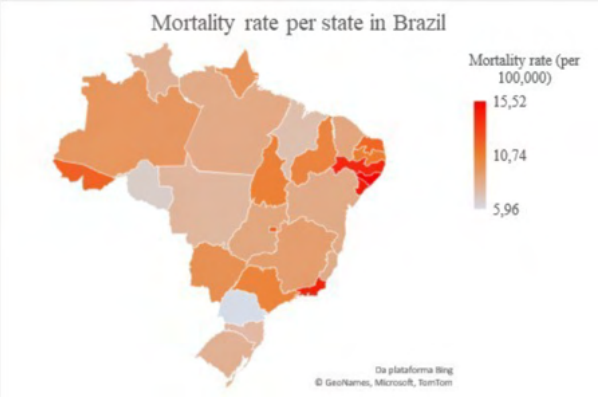

Fig.1: Mean mortality rate from TBI in Brazil per state from 2009 to 2019.

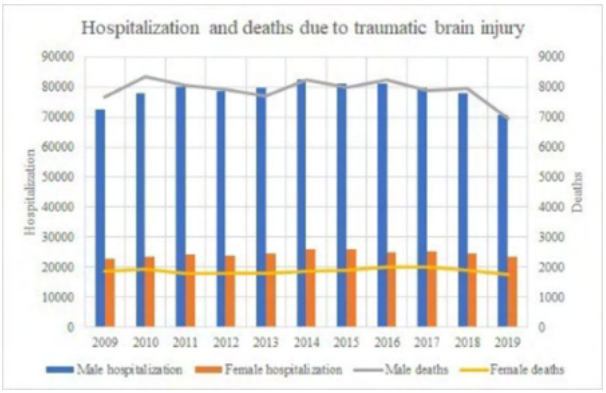

Fig.2: The difference in hospitalization and deaths between genders due to traumatic brain injury in Brazil from 2009 to 2019.

Conclusion: Over the decade, the mortality rate has remained virtually stable. We identified that there is a regional inequality in this country. Moreover, the causes of the difference in mortality from TBI between men and women in Brazil can be the subject of further studies.
Disclosure: Nothing to disclose.

EPO-494

Brazilian Epidemiological study on Traumatic Brain Injury with firearms

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[1] Manaus, Brazil, [2] Aragarcas, Brazil, [3] Maringa, Brazil, [4] Joao Pessoa, Brazil, [5] Varzea grande, Brazil, [6] Pelotas, Brazil, [7] Itabuna, Brazil, [8] Teixeira de Freitas, Brazil

Background and aims: Traumatic brain injury (TBI) occurs when external actions are able to generate an anatomical lesion or even cause impairment in the performance of the brain, skull and its structures. It is a public health problem, in which the incidence and prevalence has been increasing worldwide.

Methods: The systematized review was performed based on a cutout of the findings of both case reports, involving clinical patients, as well as research in urgency and emergence of bibliographic character and epidemiogical nature. This allowed the development of a contingency analysis on the topic. In this sense, the databases used were: (a) Scielo, (b) Urgent and emergency Newspaper, (c) PUBMED, (d) Periodicals in Neurology and Neurosurgery and, finally, (e) epidemiological reports on incidence of accidents trauma caused by firearms.

Results: Trauma caused by a firearm can also be caused by bladed weapons and metal, bone or dental fragments, which produce injuries ranging from small abrasions to extensive and severe fractures. They occur mainly in young adults aged 19 to 30 years, male, due to the greater exposure to triggering factors.

Conclusion: The epidemiology of head trauma by brain injury is given by three cases that cause a significant relationship: (a) incidence in young and black men, (b) occurrence in peripheral regions, (c) outcome, invariably, progressing to death, when affected perforating the brain organ and (d) the surgical intervention measures, urgently the rapid, planned and equivalent actions, whether in small or large centers.

Disclosure: Nothing to disclose.

EPO-495

Brainstem Auditory Evoked Potentials for Evaluation of the risk of Chronic Traumatic Encephalopathy After Mild TBI

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Background and aims: Improving the clinical diagnose of mild Traumatic Brain Injury (mTBI) through the use of early biomarkers can help us to predict patients at risk of neurodegeneration after mTBI. The conventional imaging tests CT/MRI are limited in their capacity to assess microstructural or functional damages due to mTBI. There is an increasing urgency to develop new diagnostic modalities for the accurate identification of at-risk patients. The aim of this study is to investigate changes of Brainstem Auditory Evoked Potentials (BAEP) as diagnostic and prognostic neurophysiological markers in patients with single mTBI or repetitive concussions.

Methods: 84 patients with mild TBI were included in the study: 72 patients with single mTBI, 12 patients after repetitive concussions. In all patients CT/MRI was conducted to exclude more severe TBI. BAEP were conducted in the first month after injury. BAEP follow-up was carried out on the 3rd, 6th month, one year after the trauma to 16 of them.

Results: The markers of brainstem dysfunction are found in the both groups: delayed peak latencies, abnormal prolongation of of I-III, III-V, I-V interpeak intervals, significant interaural differences, low amplitude or absence of the main BAEP waves (fig.1,2). More than one type of abnormalities were found in 17 cases.

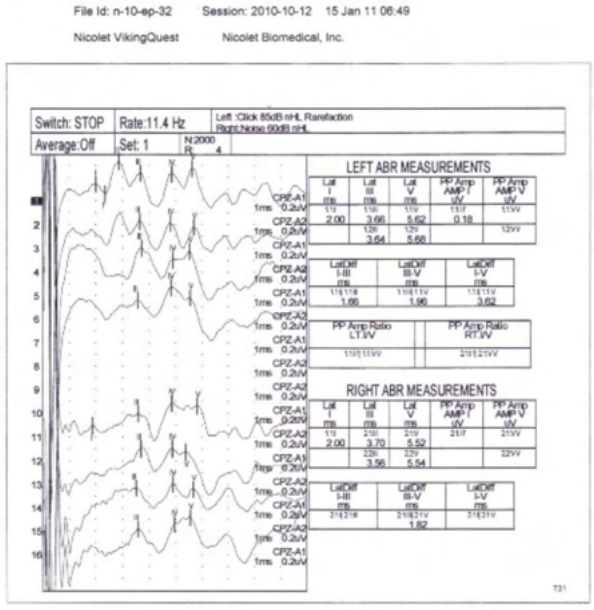

fig.1

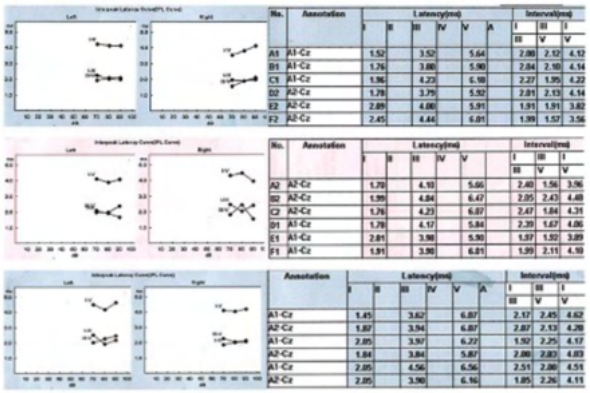

fig.2

Conclusion: BAEP can be applied as a diagnostic method in patients with CT/MRI- negative mild TBI. Persistent BAEP-abnormalities can be used as diagnostic and prognostic neurophysiological markers for incomplete recovery and the accurate identification of at-risk patients and the initiation of preventative therapy early in the disease course.
Disclosure: Nothing to disclose.

EPO-496

Thrombosis secondary to oropharyngeal trauma in child

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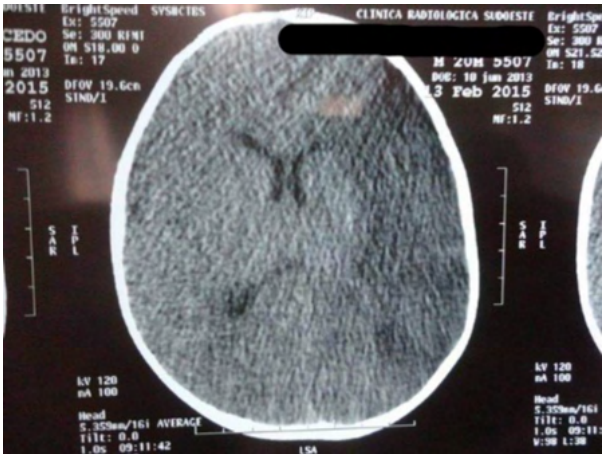
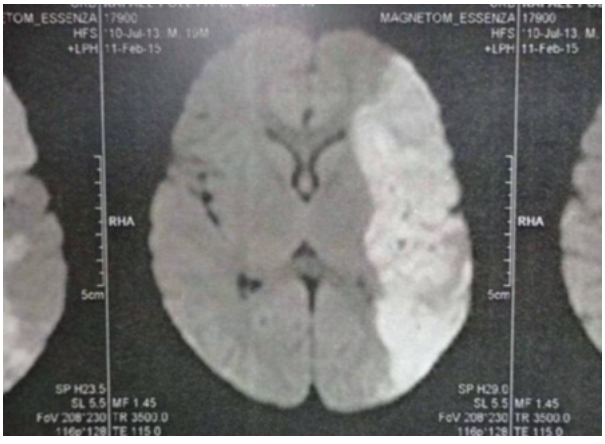
[1] Francisco Beltrao, Brazil, [2] Mafra, Brazil, [3] Neurosurgery, Pato Branco, Brazil, [4] Medical Student, Francisco Beltrão, Brazil

Background and aims: Intraoral injuries are common in childhood and, although rare, the possibility of neurological complication in these cases cannot be ignored. The most common mechanism is vascular injury due to compression of the internal carotid artery (ICA) against the bone, causing thrombogenesis.
Methods: This study aims to report a case of thrombosis of ICA for oropharyngeal trauma.
Results: Mr. R. M., male, 19 months old, previously healthy, was admitted to the hospital with history of fall from own height 7 hours ago, causing palatal trauma for pencil in the oral cavity. He presented slumber, right hemiparesis, and crying when stimulated. He had been attended at other health unit to suture the palate, with no neurological deficits at that moment. After ictal episode at home, he was referred to hospital care. Blood count and cranial Computed Tomography (CT) were normal. Magnetic Resonance Imaging showed ischemic lesion at MCA territory, and Transcranial Doppler revealed intimate layer lesion of the ICA and MCA. Another cranial CT exhibited ischemia of MCA territory. Three years after the incident, the patient's neuropsychological tests are normal, but he has mild strenght deficit in right dimidium and is now left-handed – because of changing the dominant hemisphere.



2nd cranial CT showing erasure of ventricles, midline deviation and hypodensity in left MCA territory



MRI showing hypointensity in left MCA territory

Conclusion: Diagnosing childhood stroke demands knowledge of the base cause and high suspicion. Time is a key-factor, because four to 48 hours runs between formation and embolization of the thrombus, causing delayed onset of symptoms. It is important to inform the family about warning signs, orienting them to return to the hospital if needed.
Disclosure: The authors have no conflicts of interest to report.

EPO-497

Long-term neurological consequences of high-energy combat injuries

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Background and aims: Long-term hostilities in eastern Ukraine have resulted in military casualties, numerous injuries to population of our country.
Methods: Neurological examination of 391 patients with combat trauma to bones, joints of extremities, operated at Institute in long-term period was performed. 68% of individuals had medical history of mine-explosive injuries (MEI), 32% of gun-shot injuries (GSI).
Results: In conditions of mine-explosive injuries (MEI), damage of upper, lower extremities was more often combined at left side. Multiple fractures of bones of extremities were diagnosed, mainly in distal parts. Large joints were often damaged, leading to limb contractures. In conditions of gun-shot injuries (GSI), damage to bones of extremities was more isolated, but such soldiers were more likely to have unconsolidated fractures of bones of forearms, legs, feet. 12 soldiers had radial clubhand. Radial nerve was damaged in 59 soldiers, median nerve in 73 soldiers, ulnar nerve in 84 soldiers, combined damage to ulnar and median nerves in 19 patients. 74 soldiers had injuries to main branch of sciatic nerve; injuries to fibular nerve was diagnosed in 41 people and tibial nerve – in 10 people. Asthenovegetative syndrome was found in 72% individuals; cognitive impairment in 46% patients with MEI, 33% with GSI; 32 individuals with MEI, 27 individuals with GSI - depressive disorders.
Conclusion: In long-term rehabilitation period, patients who have military injuries as bone injuries, joints damages often require corrections of neurological disorders.
Disclosure: Nothing to disclose.

EPO-498

Right Vertebral Artery dissection associated with right occipital lobe ischemia due to car accident: case report

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Background and aims: The vertebral arteries are vessels that emerge from the subclavian arteries, they depart towards the brain through the transverse foramen of the neck vertebrae. These unite in the region of the brain stem forming, together with the basilar artery, the vertebrobasilar system , responsible for irrigating structures such as the cerebellum, occipital lobes, and brain stem. Some traumas, particularly in the neck, can generate dissection of the vertebral arteries, contributing to the formation of thrombi and culminating in ischemic events.
Methods: It consists of a case report of a male patient, victim of an automobile accident (motorcycle) two days ago. The patient sought the emergency unit with complaints of severe pain in the clavicle region and homonymous hemianopsia on the left. Computed tomography (CT) examination of the skull that showed the presence of ischemia in the right occipital lobe, and this finding was confirmed by magnetic resonance imaging (MRI). Arteriography: no significant changes. The patient was referred to the orthopedics center receiving the necessary care.

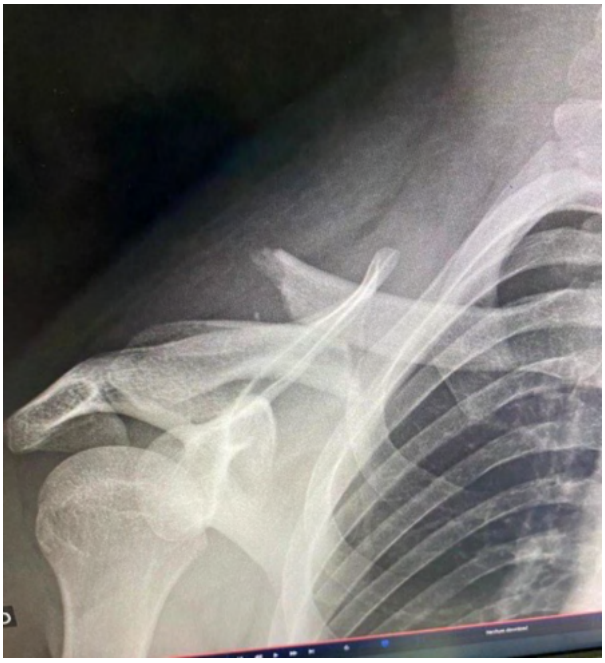

IMAGE 1. X-ray examination showing fracture of the clavicle

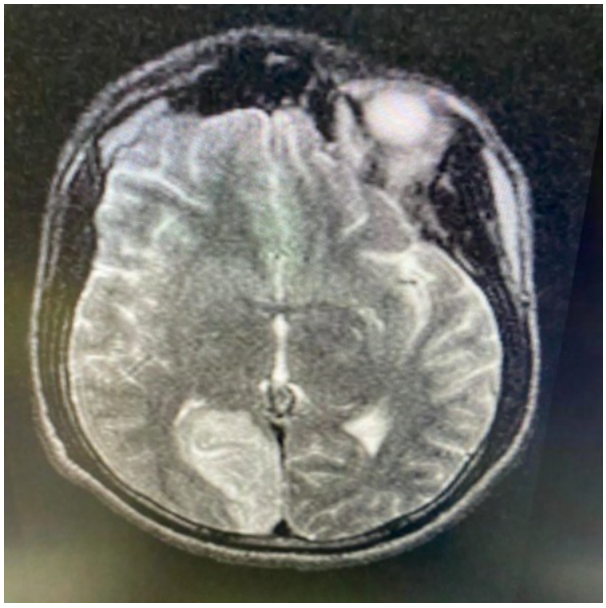

IMAGE 2. Magnetic resonance imaging showing ischemia in the right occipital region

Results: In the case in question, we have a patient with a history of trauma. The topography of the trauma corresponds exactly to the path of the vertebral artery, suggesting a causal relationship between the trauma and the dissection. In addition, the ischemic area in the right occipital lobe supports the hypothesis of an ischemic event affecting the vertebrobasilar system.
Conclusion: The neurological evaluation of a patient who is the victim of an automobile accident is extremely relevant, given the cerebrovascular repercussions that can occur.
Disclosure: Yes

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EPO-499

Neurofibromatosis type 1 and moyamoya syndrome: neuropsychological impact before and after surgery

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Background and aims: Neurofibromatosis type 1 (NF1) is one of the most common neurological autosomal dominant conditions, and an associated vasculopathy is a frequent but often under-recognized complication.
Methods: Case Report
Results: A 34-year-old man, graduated in public relations, with NF1 diagnosed in adolescence, was referenced to Neurology at the age of 27. Brain angio-MRI revealed a segmental stenosis in the anterior circulation, with a compensatory leptomeningeal circulation. Transcranial/cervical ultrasound suggested a progressively occlusive vasculopathy, as in moyamoya syndrome, confirmed by cerebral angiography. At that time, the patient was clinically asymptomatic. One year later, follow-up angio-MRI revealed an important and progressive caliber reduction in the supraclinoid internal carotid and middle cerebral (M1) arteries, with no flow in the anterior cerebral arteries. SPECT scan showed a moderate hypoperfusion in the left cerebral hemisphere, right frontal and temporal lobes. Neuropsychological assessment revealed slight difficulties in mental calculus, visual reproduction, and executive domains, suggesting a predominantly executive mild cognitive impairment. Given the imaging progression, he was submitted in september 2016 to an anastomosis of the superficial temporal artery to right M3 branch, and an encephaloduromyosinangiosis. Post-surgical neuropsychological assessment showed a significant improvement in visual memory and information processing speed tests. Due to progressive disease in the left anterior circulation he underwent a left encephaloduromyosinangiosis in march 2020.
Conclusion: Moyamoya syndrome is a rare cerebrovascular condition, which incidence is increased in NF1. This case illustrates its incidental diagnosis, the neuropsychological impact of the association of these diseases, as well as the importance of the surgery in these cases.
Disclosure: Nothing to disclose.

EPO-500

Prognosis beyond the six-hour window for Mechanical thrombectomy

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Background and aims: Since 2018, recommendations for mechanical thrombectomy (MT) were extended beyond six hours after symptom-onset according to criteria from DAWN and DEFUSE-3 studies. We aim to analyze functional/vital outcome of stroke patients undergoing MT after six hours.
Methods: Retrospective analysis of MT performed in 2018-2019. Demographic, stroke, MT and one-year follow-up data were collected, and inferential statistical analysis was applied.
Results: From 268 MT, 67 patients were treated beyond six hours, 33 (49.25%) male, median age 75. 60 (89.6%) had pre-stroke mRS<2; 64 (95.5%) NIHSS6; 47 (70.2%) anterior circulation occlusion, 46 (97.9%) with ASPECTS6. Median time of symptoms-to-groin was 7.6 hours. 18 (26.9%) patients repeated imaging for treatment decision. A total of nine (13.43%) died at discharge, and 24 (35.8%) at one-year. 13 (24.53%) had mRS<3 at discharge and 11 (21.6%) at one-year. Comparing with those within the six-hour window, these patients were younger (median 75 vs. 78 years, p=0.045); received thrombolysis less often (31.3% vs. 65.9%, p=0.001); and less often had anterior circulation occlusion (70.2%, vs. 89.7%, p=0.001). However, there was no significant difference in functional/vital outcome. Predictors of one-year death were age >75 (48% vs 25%, p=0.047) and previous disability (80% vs. 30%, p=0.041). Posterior circulation occlusion had higher mortality (35% vs. 4.3%, p=0.002) at discharge.
Conclusion: MT patients treated after the six hour-window were younger, had more often posterior circulation occlusion, but still benefited from treatment. Few did additional imaging, required by the aforementioned studies, which is less available. Selection bias may explain the differences we found.
Disclosure: Nothing to disclose.

EPO-501

Pseudo-ulnar palsy due to cardioembolic cortical infarction

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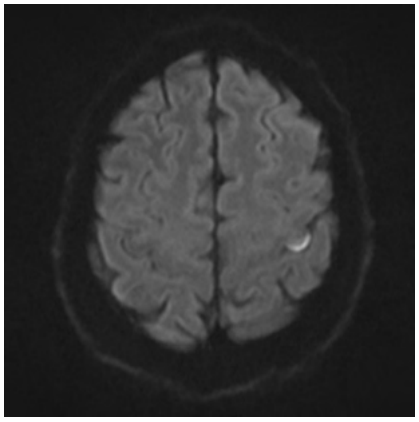
Background and aims: Small cortical strokes may cause predominant weakness restricted to a particular group of muscles, that can mimic peripheral nerve palsy. We present a rare case of pseudo-ulnar palsy caused by a small embolic stroke in the precentral knob.
Methods: Case Report.
Results: A 43-year-old nonsmoker man, with no medical history, presented in the emergency department with a claw hand sign developed three hours ago, since his morning wake-up. Neurological examination, revealed weakness of the right abductor digiti minimi, flexor digiti minimi and opponens digiti minimi muscle, as well as the right palmar and dorsal interosseous, lumbrical and flexor digitorum profundus muscles of the forth and fifth finger. Other muscles of the thenar and hypothenar were spared. No other abnormal finding was noted. Although the muscle weakness was suggestive of ulnar compression at Guyon's canal, the acute onset of the palsy doubted the diagnosis and a brain magnetic resonance imaging was performed. Surprisingly an acute cortical infarct in the left precentral knob was discovered. Extended work-up revealed a tunnel-like patent foramen ovale with a positive right-to-left shunt, as a cause of stroke. Evaluation for acute deep venous thrombosis or venous thromboembolism was negative. The patient recovered within a week and a PFO device closure was scheduled on top of antiplatelet treatment.



Diffusion Weighted Imaging (DWI) with high signal in the left precentral knob indicating acute infarct.

Conclusion: Acute ischemic distal arm paresis is extremely rare, especially when there is a particular nerve distribution. In palsies with acute onset, even though symptoms may seem strictly attributed to a peripheral nerve impairment, acute brain ischemia must be ruled out.
Disclosure: Nothing to disclose.

EPO-502

Effect of MTHFR C677T on homocysteine and folate levels in young ischemic stroke patients

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Background and aims: The polymorphisms MTHFR C6777T is a key regulatory enzyme in folate and homocysteine metabolism which are an independent risk factor for ischemic stroke. The aim of our study is to assess the effects of polymorphisms methylenetetrahydrofolate reductase reductase (MTHFR) on serum homocysteine (Hcy) and folate levels.
Methods: We recruited ischemic stroke patients in the department of Neurology from March 2016 to June 2020. The MTHFR C677T polymorphism was genotyped using polymerase chain reaction-restriction fragment length polymorphism analysis. Folate and Hcy concentrations were determined by the fluorescence polarization technique (FPIA).
Results: We include 109 patients, with a mean age of 39.6 ±6.5 and a sex ratio equal to 1.4, Men had significantly higher serum Hcy concentrations than women (p=0.04), the mutation was detected in 65 patients about 75,3% are heterozygous and 24.6% are homozygous for the variant C677T. Individuals with the MTHFR TT genotype had significantly higher serum Hcy concentrations than individuals with the CC and CT genotypes (p<10-3). a more folate deficiency observed with the TT genotype than in individuals with the CC genotype (p<10-3).
Conclusion: MTHFR C677T polymorphisms are major factors influencing folate status. Individuals with the TT genotype have lower serum folate concentrations and higher serum Hcy concentrations than those with the CC genotype. appropriate doses of folic acid and vitamin B12 supplementation could help normalize the blood level of Hcy, particularly in individuals with the MTHFR 677TT genotype.
Disclosure: KEYWORD: MTHFR C677T, ischemic stroke, homocysteine, folate.

EPO-503

Association between polymorphisms MTHFR (C677T, A1298C) increase risk of ischemic stroke in young adult

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Background and aims: The gene for five, 10-methylenetetrahydrofolate reductase or MTHFR gene encodes protein methylenetetrahydrofolate reductase (MTHFR), an important enzyme in folate metabolism. It has a heterogeneous worldwide distribution and is associated with various pathologies, including ischemic stroke (IS). The aim of our study is to establish a causal link between tow polymorphisms of MTHFR (677C>T and 1,298A>C) in a young Tunisian population with IS.

Methods: One hundred and sixty-one patients <50 years with IS and 114 controls were tested for the 677T and 1,298C polymorphisms in the MTHFR gene. Molecular analysis was performed by the PCR-RFLP method.

Results: We collected 161 patients and 114 controls, matched in sex and age. Molecular exploration showed that the MTHFR 677T and 1,298C polymorphisms were both more frequent in patients than in controls (p<10-3). The compound genotype of CT/AC revealed a 4.98-fold increased risk for IS (OR: 4.98; 95%CI [2.016–12.336]).

Conclusion: Our case-control study confirmed the major involvement of MTHFR polymorphisms in the occurrence IS (individually or in concert). This polymorphism is considered as an important risk factors for stroke in Tunisian young adults.

Disclosure: Key worlds: Ischemic stroke, young adult, MTHFR C677T, MTHFR A1298C.

EPO-504

Cu/Zn molar ratio in the serum of patients with acute ischemic stroke (AIS) in northeastern Poland- preliminary study

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Background and aims: Copper(Cu) and zinc(Zn) are essential micronutrients and components for the development of the immune and antioxidative defense system. High serum Cu/Zn molar ratio is associated with a higher risk of cardiovascular mortality and is used as a marker of oxidative stress burden. The aim of this study was to estimate the Cu/Zn molar ratio in the serum of patients with AIS in northeastern Poland.

Methods: 126 patients with AIS (mean age 69.3±10.95 years), as well as a control group of 50 healthy volunteers (mean age 53.9±15.81 years) were examined. The serum concentrations of mineral components were determined by atomic absorption spectrometry method. The molar ratio of Cu/Zn was assessed. Clinical parameters were updated based on medical records.

Results: Significantly higher values of Cu/Zn molar ratio were observed among patients with AIS (Median:1.67; Q1= 1.21; Q3=2.16) than in healthy control subjects (Median:1.39; Q1=1.09; Q3=1.78) (p=0.05). We observed a correlation between Cu/Zn molar ratio and: NIH Stroke Scale in admission, lesion volume on head neuroimaging in the study group (r=0.21, p=0.017; r=0.37, p=0.00004 respectively). No statistically significant differences were observed in Cu/Zn molar ratio in relation to sex, age, smoking status, TOAST classification (the highest values were observed in cardioembolic strokes, Median:2.09), administered treatment (intervention therapy compared to conservative) in patients with AIS (p=0.55; p=0.82; p=0.10; p=0.007; p=0.51 respectively).

Conclusion: Our results demonstrate that imbalance of metal homeostasis seems to play a crucial role in the pathogenesis of AIS. Disruption of the serum Cu/Zn molar ratio may be a favorable indicator of nutritional status and oxidative stress in patients with AIS.

Disclosure: Nothing to disclose.

EPO-505

Cerebral arteriovenous malformation-related Amyotrophic Lateral Sclerosis: a case report

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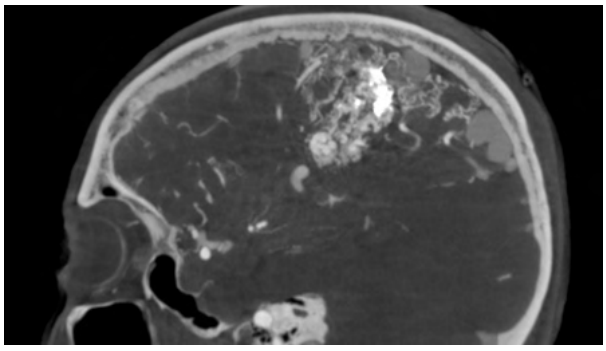
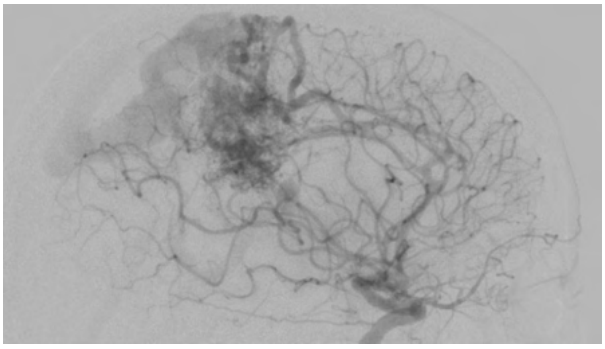
Background and aims: Previous reports have suggested that for a subgroup of cerebral arteriovenous malformations (AVMs) with rare architecture and significant perinidal angiogenesis, multiple partial embolisations are associated with an increased risk for developing Amyotrophic Lateral Sclerosis (ALS) at an unusually young age.
Methods: We report the case of a 40-year-old woman with a large right prefrontal gyrus AVM, who developed ALS 19 years after the first embolisation.
Results: Our patient had a history of 2 partial embolisations of the AVM, the latter of which was complicated with ischemia and left side hemiparesis. She also had a history of hydrocephalus with shunt valve placement. 19 years after the first embolisation, she presented with worsening left side hemiparesis and bulbar symptoms of insidious onset. She consequently underwent a third partial embolisation of the AVM. However, as the symptoms progressed, a neurological evaluation was sought 2 months later. Clinical and electromyographic (EMG) evaluation revealed upper and lower motor neurone involvement in three regions. Workup, including autoimmune panels, cancer screening, CSF analysis and M.Gravis autoantibodies, was unremarkable. Brain neuroimaging was unchanged. The patient met the Awaji criteria and a diagnosis of definite ALS was made. She was started on riluzole and underwent a gastrostomy due to precarious swallowing. The patient deteriorated quickly and died three months after receiving the diagnosis.



Saggital section of three-dimensional angiography: part of the embolic agent and profuse perinidal angiogenesis are seen



Digital Subtraction Angiography of the Left Internal Carotid Artery: diffuse contrast enhancement pattern with presence of multiple en passage vessels

Conclusion: Our report adds to the few known cases of ALS developing in patients with embolisation treatment of cerebral AVMs. Close follow-up of patients with similar background could help elucidate the mechanisms of this correlation.
Disclosure: Nothing to disclose.

EPO-506

COVID-19 indirectly hits stroke patients, as hospital discharges in Romania see a dramatic decrease during the pandemic

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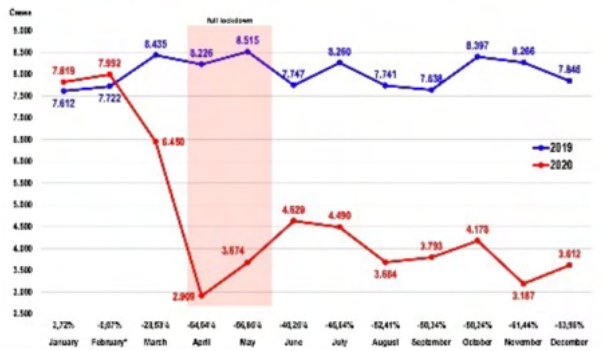
Background and aims: SARS-CoV-2 has reshaped the healthcare delivery pathways around the world. The high burden on secondary and tertiary care capacity and several mobility restrictions have forced restriction or deference of treatment for most patient groups, to a mostly unexplored extent. Driven by the hypothesis that underfunded health systems such as Romania have become disproportionately weak due to these changes, and based on reports of patient access barriers, we examined the number of neurology ward discharges national level before and during the pandemic.

Methods: Monthly reimbursement data from the Romanian Diagnoses Related Groups (RO-DRG) was used to identify monthly discharge totals from acute neurology wards and stroke groups (B3111-B3114), from private and public hospitals in contract with the Romanian National Health Insurance House. We report crude cases, as well as proportional differences between 2019 and 2020.

Results: Neurological ward discharges dropped as much as 65% in 2020 compared to the previous year, during the country-wide lockdown (Figure 1). A nearly similar trend has been observed for stroke, which in theory is prioritized due to the high burden and importance of acute care for overall patient outcomes (Figure 2). In total, Romania discharged 71,612 fewer patients on acute neurology wards in 2020 vs. 2019, of which 56% were stroke patients.



RO-DRG discharge trends for Neurology wards in Romanian hospitals

Discharge trends for RO-DRG stroke groups B3111-B3114 in Romanian hospitals

Conclusion: The decrease in discharges for acute care neurology wards in Romania during the COVID-19 pandemic is worryingly high. Romanian stroke patients continue to be denied access to essential acute care and neurorehabilitation, even after the country's full lockdown has been lifted.

Disclosure: Nothing to disclose.

EPO-507

In hospital stroke mortality: retrospective cohort study in Republic of Moldova`s tertiary neurology center

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Background and aims: In-hospital mortality is a well-known stroke care quality indicator influenced by many different factors. The aim of the study was to characterize stroke care in a stroke unit.
Methods: Retrospective medical records evaluation of all strokes from the electronic institutional data registry from January 2018 till January 2020 was performed. The mortality rates were calculated and compared with those from the RES-Q registry.
Results: Was identified 2,602 records of stroke patients, 1,979 with ischemic stroke (76.05%) and 623 with hemorrhagic stroke (23.9%). The study cohort includes 1,199 women (46.07%) and 1,403 men (53.9%), 919 women with ischemic (46.4%), and 280 with hemorrhagic one (44.9%). Overall, in hospital stroke mortality was 16.21%, for ischemic stroke – 12.88% and for hemorrhagic – 26.8%. When stratified by ICD 10 codes the mortality rates for embolic stroke (I,634) were 16.25% and for thrombotic (I,633) – 12.51%. The mortality rates for hemorrhagic stroke were: 73.9% for brainstem localization (I,613), 60% – in hemisphere, unspecified (I,612), 48.71% – intraventricular (I,615), 33.33% – cerebellum (I,614), 22.22% – in hemisphere, subcortical (I,610), 18.33% – in hemisphere, cortical (I,611) and 25.4% – SAH (I60). The RES-Q registry gave an overall in-hospital stroke mortality rate of around 22% with is different from our electronic data registry and could be explained by registry methodology.
Conclusion: In-hospital stroke mortality rates are high compared to other countries that indicate the urgent need to explore the determining factors and expand the stroke care quality monitoring and management.
Disclosure: The study is a part of national project 20.80009.8007.39.

EPO-508

Hemi-orolingual angioedema due to IV Alteplase administration for acute ischemic stroke in a patient treated with ACE-I

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Background and aims: orolingual angioedema is a rare, but potentially life-threatening complication of recombinant tissue plasminogen activator (rtPA) administered in acute ischemic strokes. Some of the patients present contralateral swelling, referred as "on the opposite side of the hemiparesis". It appears that patients treated previously with ACE-Inhibitors may be at an increased risk of developing angioedema after rtPA administration.
Methods: The aim is to present the case of a rare and major complication of Alteplase administration in a patient treated with Enalapril iv before the initiation of the thrombolysis.
Results: Case report: an eight years old right handed female presented in the Emergency Department with acute ischemic stroke, with one hour onset. The NIHSS scale was 11 points. In order to proceed with the administration, because of the high blood pressure, an iv Enalapril was administrated. 10 minutes after the thrombolytic therapy ended, the patient presented right hemi-orolingual edema, the swallowing being noticed by the medical staff and not as a complaint from the patient. In the absence of airway obstruction, medical treatment was performed and the patient was closely observed.
Conclusion: the incidence of angioedema secondary to Alteplase administration increases with the use of ACE-I. In the Covid-19 Pandemic period, it is important to anticipate any possible complications, when patients are wearing a facial mask, in order to act promptly.
Disclosure: Nothing to disclose.

EPO-509

The cost-benefit of treating patients with post-stroke spasticity with botulinum toxin type A

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Background and aims: Post-stroke spasticity directly impacts quality of life. The use of botulinum toxin type A as a therapeutic alternative proves to be clinically effective, however, economically, still little analyzed. Thus, the aim of this study is to compare and interpret the cost-benefit of treatment with and without the toxin.
Methods: This is a systematic review with searches made in the databases of Pubmed/Medline, Scielo, Web of Science and LILACS, using the descriptors "Botulinum toxin" AND "stroke" AND "spasticity" AND "cost" OR "Cost-effectiveness", related to adult humans, published between 2011 and 2021, in English and Portuguese.
Results: Of the 34 articles found, one clinical trial and five observational studies were included. The studies pointed to an increase of up to 93.48% in the therapeutic cost when opting for the use of botulinum toxin type A, however, in one of the observational studies, there was a 4.94% reduction in the total cost, if we consider the lower spending on caregivers. Finally, all the articles reviewed showed an increase in QALYS (Quality-Adjusted Life Years) and ICER (Incremental Cost-Effectiveness Ratio) compared to treatment without the toxin, thus showing a better cost-benefit ratio.
Conclusion: Treatment with botulinum toxin type A for patients with post-stroke spasticity proved to be more expensive. However, the positive relationship between ICER and QALYS from the different periods and regions observed favors the option for treatment with the toxin.
Disclosure: Nothing to disclose.

EPO-510

Sex differences in risk of myocardial infarction and stroke in population aged 25–64 years with job stress in Russia

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Background and aims: To determine gender differences of cardiovascular risk over 16-years of follow-up in an open population with job stress.
Methods: Under the third screening of the WHO MONICA-psychosocial program random representative sample aged 25–64 years was surveyed in Novosibirsk in 1994 (n=1,346, 48.8% males). Stress at work was assessed by means Karasek scale. New-onset cases of myocardial infarction (MI), stroke were identified from 1994 to 2010. This longitudinal survey performed in frame budgetary issue # AAAA-A17-117112850280-2.
Results: A high level of stress at work was in 29.5% of men and in 31.6% of women (n.s.). The risk of MI over 16-years period in persons experiencing stressful situations at work was as follow: in men HR=3.592 and women HR=3.218 (95%CI 1.146–9.042); stroke risk was in men HR=2.603 (95%CI, 1.06–4.153) and in women HR was 1.956 (95%CI 1.008–3.795). In multivariate analysis risk of MI in men was HR=1.15 (95%CI 0.6–2.2) and in women HR=2.543 (95%CI 1.88–7.351); risk of stroke in men was HR=3.8 (95%CI 1.6–8.8) and in women it was HR=1.95 (95%CI 0.984–3.887). The risk of stroke was higher in those men who are living alone, divorced and widowed HR=4.2 (95% CI 1.5–13.2) and in women with lower education degree HR=3 (95%CI 0.852–11.039).
Conclusion: A high level of stress at work is not gender-specific. The risk of MI incidence over a 16-years period is higher in women than in men but stroke in men; the risk of myocardial infarction and stroke is affected by the social gradient in both genders.
Disclosure: Nothing to disclose.

EPO-511

Epidemiology of intracranial haemorrhage in Brazil: an ecological study

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Background and aims: According to Advanced Medical Life Support (AMLS), only 20% of patients who have suffered from intracranial haemorrhage recover their full functional independence. Therefore, the present study aims to expose the epidemiological profile of intracranial haemorrhage in Brazil.
Methods: Ecological study, with secondary data published by the Ministry of Health through DATASUS and extracted from the SUS Hospitalization System (SIH/SUS). The period selected was from January 2009 to December 2018 . The data included hospitalizations for intracranial haemorrhage, the total costs and deaths. Also, information about the year of service, the most affected age group and the average length of stay were analysed.
Results: There were 306,693 hospitalizations, with a total cost of R$ 1,129,812,699.40, average length was 10 days and 70,246 deaths registered. The most affected group was 55–59 years (33,668 hospitalizations), however, the highest average length was for children under one year, and the highest record of deaths for the group of 80 and over. In the analysis by year, 2011 registered most of the hospitalizations (36,643), which reduced in the following years, specially in 2012, 4,945 cases less than the previous year.
Conclusion: The data revealed a highest average of hospitalizations between the age of 55–59 years, which according to the literature can relate to the higher risk of intracranial haemorrhage in adults. Although, the superior average length of stay for children under one year may result from the complications severity. Also, the higher number of deaths in the group of 80 and over can be associated with physiological decline
Disclosure: Nothing to disclose.

EPO-512

The falling teacup: a curious stroke case

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Background and aims: The hand motor territory is located in the precentral gyrus behind the intersection of the superior frontal and precentral sulcus. There is controversy on whether the somatotopic representation of each finger in this location is separated or if there is an overlap.
Methods: .
Results: A 63-year-old hypertensive male presented to our hospital after sudden onset right index finger weakness that left him unable to hold his morning teacup. He reported a history of left middle cerebral artery ischemic stroke, of undetermined etiology. Upon admission, besides residual aphasia and right central facial palsy (sequelae), he was not able to fully extend, adduct, and abduct his right index finger. Due to the minor neurologic deficit, he was not indicated for acute reperfusion therapy and was admitted in the Neurology ward. A brain MRI revealed a minor acute ischemic lesion on the left precentral cortex, in the hand knob (HK) area. To date, no etiology was found for this event and he was discharged, with improvement of the mentioned deficits.
Conclusion: HK strokes are an uncommon stroke entity, often associated with a potential embolic mechanism. This case reports an isolated acute finger paresis due to a vascular injury of this territory. HK infarctions can present with isolated hand weakness, having different patterns of involvement. In our patient, the exclusive involvement of the right index finger after a vascular injury helps to strengthen the existence of an individual somatotopic representation of hand fingers in the human motor cortex.
Disclosure: Nothing to disclose.

EPO-513

Switching across direct oral anticoagulants: a real-life-setting pilot prospective study

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Background and aims: Crossover between direct oral anticoagulants (DOACs) has been underinvestigated, but happens frequently in clinical practice. The purpose of this study was to evaluate causes, rates and outcomes of a DOAC-to-DOAC switch.

Methods: Patients receiving their first DOAC prescription at the Anticoagulation Center, Cardiology Dept, Bologna-Bellaria Hospital in 2017–2018 were consecutively included and prospectively followed up. DOAC-to-DOAC switch was the main outcome; causes of switch (cardiovascular events and noncardiovascular drug-related adverse events) had direct biannual assessment before and after the switch.

Results: Among 300 patients enrolled (mean age 79.3 years, mean follow-up=1.5 years), with no difference in cardiovascular risk factors depending on index DOAC, 13% underwent DOAC-to-DOAC switch, minor bleeding and noncardiovascular adverse events being the most frequent causes. Dabigatran carried a three-fold increase in risk of switch compared with other DOACs, but the mean age of patients who switched was 83. Factors leading to switch resolved in 87% of cases afterwards. Annual rates of cardiovascular/noncardiovascular V events did not differ before and after the switch.

Conclusion: DOAC-to-DOAC switch happens in 9% of patients using DOAC each year, and seems not to impact rates of cardiovascular events after switch. Dabigatran, in the elderly, might be associated with a higher risk of DOAC-to-DOAC switch. Further studies are needed to confirm the long-term safety and effectiveness of switching paradigm.

Disclosure: Nothing to disclose.

Clinical neurophysiology 1

EPO-514

Cutaneous silent period in patients with amyotrophic lateral sclerosis

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Neurology, Moscow, Russian Federation

Background and aims: Cutaneous silent period (CuSP) is a brief suppression of voluntary contraction that follows strong electrical stimulation of a cutaneous nerve. CuSP has been shown to change mainly in the peripheral nervous system disorders. The aim of this study was to evaluate CuSP in patients with definite amyotrophic lateral sclerosis (ALS) according to El Escorial criteria (2000).
Methods: In order to obtain CuSP, electrical stimuli were applied through ring electrodes on the index finger. Stimulation intensity was chosen individually by multiplying sensory threshold by 20. The patient was asked to maintain a steady muscle contraction while 10 stimuli were applied. Recordings were made from the abductor pollicis brevis muscle and then averaged for further analysis.
Results: 41 patients with ALS and normal nerve conduction studies (disease duration from three to 61 months) were enrolled in the study. 20 patients had spinal-onset ALS, 21 – bulbar-onset ALS. The control group consisted of 34 age– and sex-matched healthy subjects. Both CuSP duration and end latency were markedly prolonged in patients with ALS in comparison to healthy controls ($p<0.05$). There were no statistically significant differences between CuSP parameters of patients with different sites of ALS onset. CuSP duration demonstrated positive correlation with disease duration (r=0,828) and negative correlation with ALSFRS-R (r=-0,838).
Conclusion: CuSP duration and end latency were prolonged in ALS patients in comparison to healthy controls, which could be caused by disrupted supraspinal mechanisms in ALS. Our findings suggest that CuSP capabilities in evaluating central nervous system disorders are yet to be understood.
Disclosure: The authors have no conflicts of interest to declare.

EPO-515

Assessment of patients with winged scapula: An Institutional Electrodiagnostic Experience

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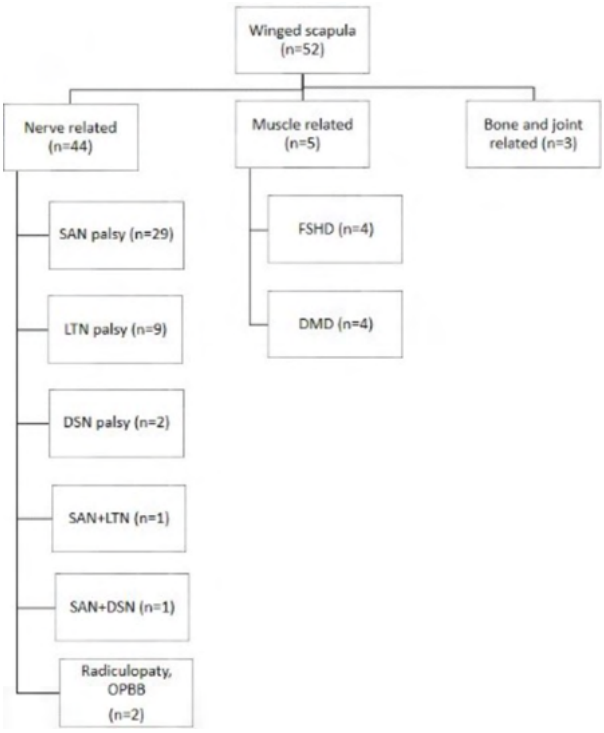
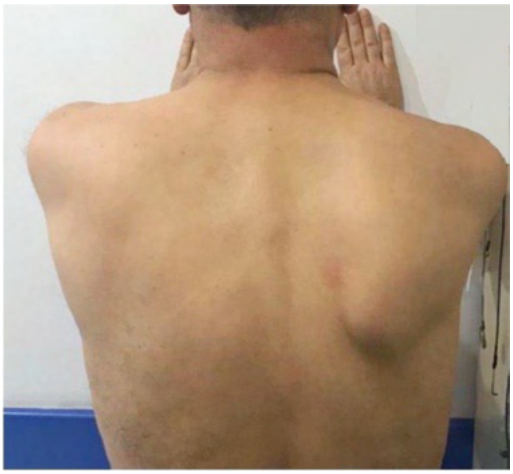
Background and aims: Winged scapula (WS) is a clinical definition and it can lead pain, functional disability and cosmetic deformity. Unilateral or bilateral WS occur due to various neurogenic and non-neurogenic etiologies. Underdiagnosis of WS and misdiagnosis of WS causes are not rare. History, physical and electrodiagnostic examination (EDX) help to accurate diagnosis.
Methods: Medical records and neurophysiological findings of 52 patients with WS, who visited a single electromyography unit for EDX, were reviewed between 2000–2019, retrospectively.
Results: The mean age was 39±16.6 years, 32 were male. Unilateral WS (89%) was more common than bilateral (11%) WS. According to EDX; 44 (85%) patients had neurogenic causes; 29 spinal accessory nerve (SAN) palsy (17 had surgical procedure), nine long thoracic nerve (LTN) palsy (4 had strenuous activity), 2 dorsal scapular nerve (DSN) (both neuralgic amyotrophy), one LTN and SAN (strenuous trauma), one both SAN and DSN (surgical procedure and radiotherapy), one cervical 5–7 radiculopathy (avulsion), one brachial plexopathy (obstetric trauma). Five (10%) patients had muscle related findings (4 facio-scapulo-humeral dystrophy, one Duchenne muscular dystrophia) and three (5%) patients had normal findings (mechanic causes) (Figure 1).

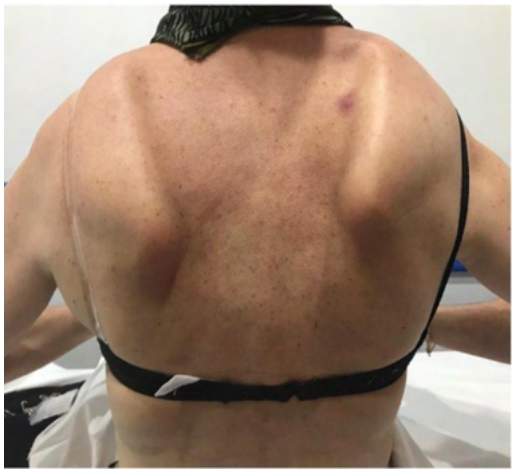


Number of patients with winged scapula according to 3 main groups and subgroups.

Conclusion: We found SAN palsy following neck surgery is the most common cause and LTN palsy (Figure 2) is the second common cause of unilateral WS. FSHD should be considered especially in bilateral WS cases (Figure 3). EDXs should be performed in WS patients to establish exact diagnosis and reveal some co-existence of WS causes that is quite difficult to diagnose them with physical examination only.



Patient had unilateral right-sided medial winged scapula due to long thoracic nerve palsy.



Patient who had diagnosed as facio-scapulo-humeral muscular dystrophy had bilateral winged scapula appearance.

Disclosure: The authors declare no financial or other conflicts of interest.

EPO-516

Neural network electroencephalograms analysis in the Parkinson's disease (PD) diagnosing problems

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Background and aims: Currently, more and more attention is paid to the search for preclinical methods for the PD diagnosis, since it has been established that the neurodegenerative process in PD begins several decades before the manifestation of the classic motor symptoms of this disease. Aim is evaluating the possibility of using Hilbert space-filling curves and convolutional neural networks together to classify electroencephalogram(EEG) signals into two groups: PD patients and a control group.
Methods: EEG signals divided into 2 groups: PD patients (n=27) and control group (n=28). The approach based on a combination of Hilbert space-filling curves and convolutional neural networks provides accuracy – 0.99, precision – 0.85, recall – 0.85, F1 measure is 0.85, which exceeds the previously presented results using the approach based on frequency analysis of EEG signals.
Results: As a result of the study, a model was obtained. This model is characterized by high performance indicators such as accuracy, precision, recall and F1 measure. The developed neural network model makes it possible to predict the development of the neurodegenerative process in patients with PD using the EEG signal.
Conclusion: The prerequisites were obtained for using a combination of space-filling curves and convolutional neural networks to analyze the EEG of persons at risk of developing PD who do not have clinical motor symptoms in order to screen the preclinical (premotor) stage of an already incipient neurodegenerative process. To improve the quality indicators of the presented method, it is necessary to increase the data sample for training the neural network.
Disclosure: Nothing to disclose.

EPO-517

Immune mediated chorea encephalopathy in childhood, a case report

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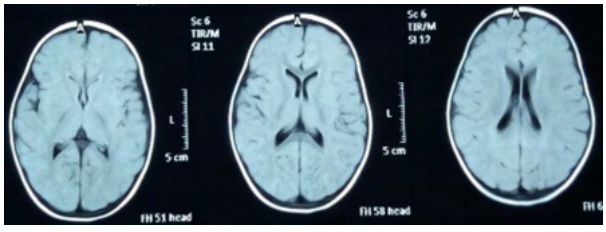
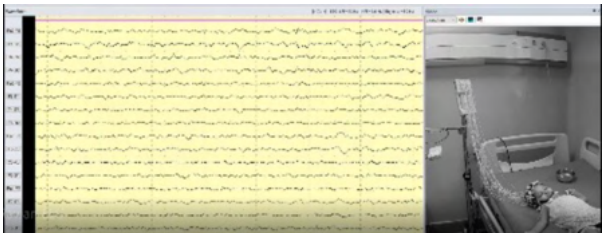
Background and aims: Movement disorder and encephalopathy in children is usually associated with either infectious or post-infectious causes; however, autoimmunity has been rarely described. We describe the clinical course of a child presented with acute hemichorea, then encephalopathy over four months.

Methods: A Previously healthy female child, 2.5 years old, without any preceding infection, or vaccination, admitted to our department with acute onset right lower limb weakness and abnormal choreic movements, followed by right upper limb. She was treated with acyclovir and ceftriaxone. Over the next week, she developed an oculogyric crisis for one hour, her mother reported outbursts of temper, crying, agitation; and hence, haloperidol and sodium valproate were added. During the next 2 weeks, chorea became generalized affecting mainly the limbs with some dystonic movements and axial hypotonia, one week later she became mute and immobile without her arousal or responsiveness being affected. MRI brain, EEG monitoring, CSF examination, extended metabolic profile were investigated.



Results: Apart from an increase of oligoclonal bands and EEG generalized slowness, there were no abnormalities. Pulse methylprednisolone, over three days was started and other medications stopped. After that, she started to show some improvement, and over the next month, she could set then stand and take some steps supported. In month three, she could walk, and start to say some brief words. 2 weeks later, she made a complete recovery.



Conclusion: This patient represented chorea-encephalopathy syndrome of a possibly immune-mediated nature, affecting the cortico-striatal circuits. The outcome appears to be very good, despite the severity of the illness.

Disclosure: Nothing to disclose.

EPO-518

Oxaliplatin- induced neuropathy and peripheral nerve hyperexcitability in a patient with gastric cancer

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Background and aims: Oxaliplatin is a commonly used platinum analogue for gastrointestinal tumors. Oxaliplatin-induced peripheral neuropathy(OXAIPN) is the most common, dose limiting, and disabling adverse effect of chemotherapy. The presentation of neuropathy induced by OXA is different from other platinum compounds, consists of acute and chronic types, that causes quite distinct pathophysiological, clinical, and electrophysiological findings.
Methods: Here, we present clinical, electrophysiological features and follow up of a patient with OXAIPN.
Results: A 53-year-old male was referred for numbness at his fingertips for about a month. He had gastric adenocarcinoma with metastasis to the liver and abdominal lymph nodes, which had been treated with a modified FOLFOX-6 regimen containing oxaliplatin, fluorouracil, and folinic-acid. Neurological examination revealed sensory impairment in a glove and stocking pattern, diminished vibration at the distal joints, and the absence of deep tendon reflexes at the ankle. During electroneuromyography (ENMG), sensory nerve action potentials couldn't be obtained, whereas motor nerve conduction studies were normal. Needle-EMG showed abundant spontaneous motor unit action potentials (MUAP), as myokymic, neuromyotonic, and myotonia-like discharges. After defining severe sensory axonal neuropathy and/or ganglionopathy and peripheral nerve hyperexcitability, FOLFOX treatment replaced, and three months later control ENMG showed mild recovery of median and ulnar sensory nerves. Spontaneous MUAP activities disappeared except for a few doublets on the first dorsal interosseous muscle that were considered as remnants of neurotoxicity.
Conclusion: ENMG has a key role in diagnosis, classification of acute/chronic neurotoxicity, and identification of reversibility, whereas follow up and research studies may enlighten the transition between these processes.
Disclosure: Authors report no conflicts of interest.

EPO-519

Early recognition of polyneuropathy by upper limb mixed nerve conduction studies among patients with type 2 diabetes

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Background and aims: In diabetes mellitus (DM) myelin-sheath dysfunction has been suggested as the earliest response to abnormal glucose metabolism. The aim of our study is the early electrophysiological detection of this dysfunction in DM patients with normal nerve conduction studies (NCS) despite having neuropathic symptoms.
Methods: Fourteen DM patients with normal sensory and motor NCS and 27 healthy individuals included to the study. For median and ulnar nerves following basic parameters were obtained; 1 – By orthodromic-stimulation of 5. digit, 2. digit and palm and recording from wrist, distal sensory nerve action potential amplitudes (Distal-Amplitude) and distal nerve conduction velocities (Distal-NCV), 2 – By orthodromic-stimulating the 5. digit, 2. digit and palm, and recording from elbow, Proximal-Amplitudes, and Proximal-NCVs, 3 – By orthodromic-stimulating at wrist and recording from elbow, Mixed-Amplitudes and Mixed-NCVs were obtained.
Results: There wasn't a significant difference between groups for age and basic parameters. However, the Distal SNAP NCV / Mixed NCV ratio was significantly decreased in DM patients which suggests myelin dysfunction at sensory fibers and normal conduction at fast-conducted motor fibers. On the other hand, the Distal SNAP amplitude / Mixed Amplitude ratio was significantly increased in DM patients. This seemingly contradictory finding is likely due to more pronounced abnormal temporal dispersion of SNAPs at longer sensory nerve segments (mixed NCS) which again supports the myelin dysfunction at these sensory fibers.
Conclusion: These NCS ratios are easy to obtain during routine NCS and can provide early detection of myelin dysfunction in DM which allows new treatment strategies and clarification of the early pathophysiological changes.
Disclosure: Authors report no conflicts of interest.

EPO-520

Dynamics of EEG power in the contralesional hemisphere in post-stroke patients

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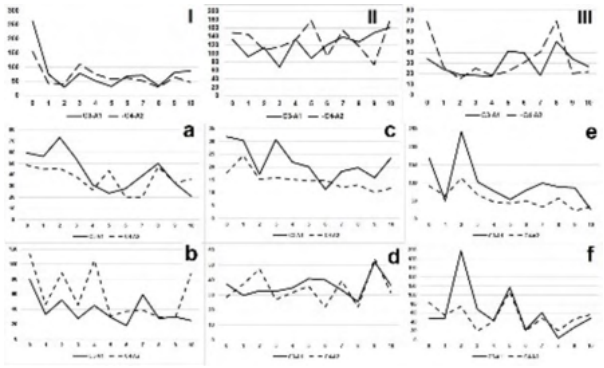
Background and aims: In poststroke patients the severity of motor disorders in nonparetic arm increases parallelly to the level of contralesional arm's paresis. The aim – investigation of bioelectric activity in the cortex of the contralesional hemisphere of the brain in patients with post-stroke paresis.

Methods: We examined five healthy right-handed people and five right-handed patients three–six months after a stroke in the left hemisphere. To assess the neuroplastic process, we used the dynamics of EEG power during the period of movement imagery (MI) in the "healthy" arm.

Results: In poststroke patients, event-related desynchronization (ERD) was initially gradually manifested by 4–5 seconds, quickly replaced by event-related synchronization (ERS). At the same time, the excitatory interaction of the primary motor cortex and the frontal-parietal regions in the affected and "intact" hemispheres was revealed. After a course of rehabilitation, ERD was clearly detected in C3, in C4 it was unstable, but it was retained until the end of MI. In prefrontal and parietal cortex of both hemispheres, the EEG power increased at 4–5 seconds.



Changes in power in the (I, a, b), (II, c, d), and (III, e, f) rhythms i(leads C3–A1 and C4–A2), V2. 0–10 - seconds of movement imagery in left hand. I, II, III) control; a, c, e) baseline measures; b, d, f) after neurorehabilitation courses.

Conclusion: Changes in EEG power after a course of neurorehabilitation can be interpreted as a manifestation of the reorganization of neural networks. There was noted involvement of the frontal and parietal zones of "mirror" neurons of both hemispheres, which may reflect the dynamic reorganization of neural networks. The power of the main EEG rhythms differed from the control group before and after rehabilitation and was not similar to the reconstruction of bioelectric activity in the affected left hemisphere.

Disclosure: This study was supported by the Russian Foundation for Basic Research (Grant No. 19-015-00192).

EPO-521

Abstract withdrawn

COVID-19 4

EPO-522

Acquired pendular nystagmus in the setting of COVID-19

M. Pereira Coutinho [1], P. Faustino [1], J. Lourenço [1], L. Leitão [2]
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Background and aims: Acquired pendular nystagmus has multiple possible etiologies, ranging from genetic disorders to an inflammatory or toxic/metabolic origin. In the past year, various neurologic manifestations have been described as associated to the SARS-CoV-2 infection. Both direct viral effects and immune-mediated phenomena arise as possible pathogenic mechanisms.
Methods: Case report.
Results: A 38-year-old Indian male, with no relevant medical or family history, was diagnosed with a non-hypoxemic SARS-CoV-2 pneumonia. Four days later, he presented with somnolence, headache with photophobia, vertigo, oscillopsia and vomiting. The neurological exam revealed a bilateral horizontal pendular nystagmus in all gaze directions, with a right gaze-evoked component. No palatal tremor or auditory click. Symptoms improved with symptomatic treatment, except for oscillopsia, due to the persistence of the nystagmus even after virologic cure. Brain 3T MRI was normal; extensive infectious and autoimmune CSF, blood and urine investigation was negative, as well as vascular, metabolic and neoplastic studies. A trial of gabapentin, clonazepam, and methylprednisolone was performed with only modest response.
Conclusion: The new-onset of central nystagmus soon after diagnosis of COVID-19 meets the proposed criteria for a probable association with this infection. The pathogenic mechanism is unclear: although the viral RNA was not detected in the CSF, a direct viral effect seems more likely given the earliness of the neurologic symptoms and the poor response to immunotherapy. The spread and discussion of similar situations is of utmost importance in order to establish more robust criteria for neurologic disease associated with SARS-CoV-2 infection and to enlighten the pathogenic mechanisms and potential treatment strategies.
Disclosure: Nothing to disclose.

EPO-523

COVID-19 related Parkinsonism

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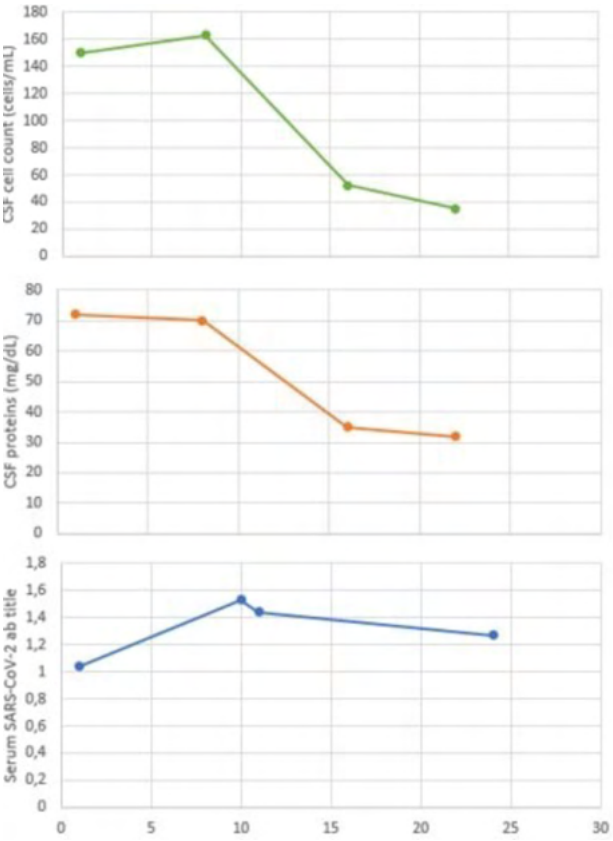
Background and aims: Infectious diseases have been linked to cases of Parkinsonism since the Spanish Flu's association with encephalitis lethargica. Recently, case reports emerged suggesting a relationship between SARS-CoV-2 infection and Parkinsonism, along with literature proposing potential pathogenic mechanisms.
Methods: Case report.
Results: A 60-year-old man with known diabetes, hypertension and alcoholism, with a 10-day history of respiratory symptoms, presented to the Emergency Room with somnolence, hypoxemia, diabetic ketoacidosis and acute kidney lesion. SARS-CoV-2 PCR (nasopharyngeal swab) was positive. Neurological examination revealed an ocular flutter and upper limb myoclonus, which etiologic investigation (lumbar puncture, head CT, anti-neuronal antibodies) was negative. He soon improved and was discharged without symptoms. 2 months later, he presented to the Emergency Room with gait difficulty, markedly worsened in the past week. Examination showed a severe akinetic-rigid parkinsonism with postural instability. Head CT had no acute brain lesions. A trial of levodopa was promptly started, with striking clinical response. A DaTSCAN was performed, revealing a decreased availability of pre-synaptic dopamine transporters on the left putamen. The remaining etiologic study was negative.
Conclusion: The tight temporal relationship between SARS-CoV-2 infection and the development of parkinsonism, together with the altered DaTSCAN, suggests a relationship with the novel coronavirus infection. Similarly to other reports, our patient developed an akinetic-rigid parkinsonian phenotype on the weeks following COVID-19. The initial concomitancy of central nystagmus, followed by parkinsonism, leaves open the possibility of a viral rhombencephalitis. Together, all these reinforce the importance of increasing and sharing the growing but yet scarce knowledge on the neurological impact of SARS-CoV-2.
Disclosure: Nothing to disclose.

EPO-524

A case of probable SARS-CoV-2-related post-infectious autoimmune encephalitis with a rise in serum antibodies title

F. Pozzi [1], V. Aprea [2], F. Santangelo [3], I. Appollonio [1], C. Ferrarese [3]
[1] Monza, Italy, [2] Sesto San Giovanni, Italy, [3] Department of Neurology, Monza, Italy

Background and aims: Recent reports have linked SARS-CoV-2 infection with para- and post-infectious autoimmune encephalitis, suggesting cytokine storm as a possible pathogenesis.
Methods: We describe a patient who developed acute encephalitis three weeks after resolution of SARS-CoV-2 infection symptoms, coincident with a rise in serum anti-SARS-CoV-2 antibodies.
Results: A 29 year-old man presented with fluent aphasia and ideo-motor apraxia since awakening in the morning, mimicking a stroke. His brain CT, angio-CT and perfusion CT were all negative; an urgent brain MRI revealed non-specific FLAIR hyperintensities. After a lumbar puncture, showing 150 lymphocytes and elevated proteins, his symptoms suddenly started improving, with complete resolution two hours later. An urgent EEG showed left temporal slow waves. A SARS-CoV-2 swab turned negative, and he was admitted to the Neurology department with antiviral and antibiotic treatment. His wife had PCR-confirmed Covid-19 infection a month before, and he experienced fever and hyposmia the following week. Over the course of a month he experienced another aphasic episode, resolved with diazepam. Serum SARS-CoV-2 antibodies title increased and decreased over three weeks; notably, serial EEG showed worsening of epileptic activity along with the rise in SARS-CoV-2 antibodies title, despite anti-epileptic treatment. A brain PET was non-significant, and his CSF parameters slowly improved only after a five days cycle of methylprednisolone. Serum anti-surface antigens antibodies and CSF SARS-CoV-2 IgG were negative.



CSF and serum parameters over time

Conclusion: The patient was discharged with double anti-epileptic therapy after exclusion of known causes of encephalitis (infectious, paraneoplastic, autoimmune); therefore, in our opinion, the most probable diagnosis was SARS-CoV-2-related post-infectious encephalitis.
Disclosure: Nothing to disclose.

EPO-525

The impact of telemedicine for patients with epilepsy during the COVID-19 pandemic

L. Requião, B. Moreno, A. Paiva
[1] *Salvador, Brazil*

Background and aims: Telemedicine has come to be widely applied in the COVID-19 pandemic, including in neurology, where it is notably used in the follow-up of patients with epilepsy, especially in the management of the disease in its chronic form. However, this tool presents numerous challenges, such as difficulty in access - particularly in resource-limited countries-, reduction of the doctor-patient alliance and the impossibility of carrying out physical examinations. Thus, this study aims to analyze the impact of telehealth for patients with epilepsy during the COVID-19 pandemic.
Methods: A search for scientific articles published in 2020 was carried out in the PUBMED database. The descriptors "COVID-19", "Telemedicine" and "Epilepsy" were used, resulting in the following research formula: "((COVID-19) AND telemedicine) AND epilepsy)".
Results: In an italian study using online questionnaires, obtaining 3,321 responses, only 6% of participants were unsatisfied with remote consultation. In a german cohort with 272 participants, few disadvantages reported were the postponements of diagnostics or therapies (5.5%), limited possibilities for interpretation of anti-seizure drugs side effects or other symptoms (5.5%), language barrier without gesture compensated communication (0.9%), and increased uncertainty due to lack of face-to-face contact (0.9%). Meanwhile, in a cross-sectional study held in Pakistan more than 90% of the caregivers of patients with epilepsy do not knew about telehealth/telemedicine.
Conclusion: Although telemedicine has preserved access to care in high income countries, there are concerns related to disparities in acess to care and the long-term impact of these changes needs further investigation.
Disclosure: The study is not receiving funding/assistance from any commercial organizations.

EPO-526

SARS-CoV-2 associated Guillain-Barre syndrome: first adult case series in Latvia

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[1] *Neurology, Riga, Latvia,* [2] *Riga, Latvia,* [3] *7. Neurology, Riga, Latvia,* [4] *Department of Neurology & Neurosurgery, Riga, Latvia*

Background and aims: SARS-CoV-2 infection is remarkable with wide spectrum associated neurological complications, though peripheral nervous system manifestations are less common. Several SARS-CoV-2 associated Guillain-Barre syndrome (GBS) cases reported appearance of the first neurological symptoms approximately 10 days afer the diagnosis of COVID-19 and improvement with intravenous immunoglobulin (IVIG) therapy.
Methods: Case series.
Results: 2 female (54 and 79 years-old) and one male (63 years-old) patient were admitted to our hospitals complaining about progressive sensory disturbances and muscle weakness in extremities. All patients had previously confirmed positive SARS-CoV-2 RT-PCR nasopharyngeal tests and respiratory symptoms for an average of 17 days. Neurological examination on admission revealed symmetrically reduced tendon reflexes, asymmetric tetraparesis and polyneuropathy-type sensory disturbances with spared cranial innervation. In male patient diagnosis was complicated by co-existing severe hyponatremia (111 mmol/L). The cerebrospinal fluid analysis showed normal cell count, but increased protein level in all cases (0,53, 0,6 and 2,1g/L respectively). Diagnosis was based on clinical examination and CSF analysis (Brighton criteria Level 2), nerve conduction studies were not performed. Both female patients underwent five plasma exchange procedures; IVIG 0,4g/kg for five days was used for the male patient. All patients were discharged with the improvement of motor and sensory symptoms to continue further rehabilitation.
Conclusion: SARS-CoV-2 infection provoke autoimmune complications with an onset of new neurological symptoms early after the respiratory illness. In previously described case reports IVIG was the treatment of choice, however our experience shows that plasma exchange is equally effective in patients with SARS-CoV-2 associated GBS.
Disclosure: We have no actual or potential conflict of interest in relation to this abstract.

EPO-527

Lumbosciatalgia as the first manifestation of COVID-19 infection

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[1] Department of neurology military hospital Tunisia, Tunis, Tunisia, [2] Departement of neurology, Manouba, Tunisia, [3] Tunis, Tunisia, [4] Department od Neurology, Tunis, Tunisia, [5] Department of Neurology, Olympique, Tunisia, [6] Ariana, Tunisia

Background and aims: The clinical course of severe acute respiratory syndrome coronavirus 2 (SARS-COV-19) ranges from asymptomatic infection to severe acute respiratory failure with multi-organ involvement. The disease can cause extra pulmonary complications such as neurological disorders which are increasingly reported in the literature.

Methods: We included in our retrospective study five patients, three women and 2 men. Clinical ,biologicall and radiological data were analyzed.

Results: The mean age of the beginning of symptoms was 44.6 years old. All of them had lumbosciatalgia as the first manifestation. Lumbosciatalgia was isolated in one case and associated with other signs in four cases. The SARS-COV-19 infection was confirmed by real-time reverse transcription (PCR). Spinal cord MRI was normal in all cases. All patients received symptomatic treatment with positive outcome.

Conclusion: Lumbosciatalgia can be the inaugural symptom of SARS-COV-19. This diagnosis should be considered in patient with lumbosciatalgia in our epidemiologic context.

Disclosure: Nothing to disclose.

EPO-528

Healthcare-associated infections in the pre- and post-COVID-19 eras in a Neurology Departament

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Background and aims: Healthcare-associated infections (HAI) are a major cause of inpatient morbimortality. Those include respiratory (RI) and urinary (UI) infections, among others (OI). COVID-19 has raised awareness about the importance of hygiene measures and respiratory etiquette, potentially reducing the incidence of HAI. We aimed to assess the impact of measures implemented or reinforced during the pandemic, on the incidence of HAI in a Neurology Department.

Methods: Retrospective comparative study of the incidence of HAI between relevant periods in 2019 and 2020. Comparisons of percentage of HAI was performed using a 2-proportion z-test. Statistical significance was defined by p-value=0.05 corrected for multiple comparisons using Bonferroni's method.

Results: Between January and July of 2019, 560 patients were admitted, with 25%HAI (11%RI, 12%UI, 2%OI) versus 519 patients and 20%HAI (10%RI, 8%UI, 2%OI) in the equivalent period of 2020. The incidence of HAI between the first three months of 2019 and 2020 was, respectively, 32% (15%RI, 13%UI, 4%OI) versus 20% (16%RI, 13%UI, 1%OI). We observed 20%HAI (8%RI, 11%UI, 1%OI) between April and July 2019 versus 19%HAI (11%IR, 6%UI, 2%OI) in the same period of 2020. No statistically significant differences were seen between any groups.

Conclusion: In a tertiary Neurology Department, there was a tendency (not reaching statistical significance from March to July 2020) for a reduction of the global incidence of HAI in 2020, mainly due to fewer UI. This reduction seems to be due to progressive improvement of global/hand hygiene measures between 2019 and 2020, rather than directly associated to masks/respiratory infections, or just the pandemic period.

Disclosure: Nothing to disclose.

EPO-529

Acute Transverse Myelitis associated with SARS-CoV-2 in a young male adult: A Case Report

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Costa Rica, Costa Rica

Background and aims: The COVID-19 pandemic is the biggest and most severe in over a 100 years. Even though respiratory symptoms are amongst the most common and representative of this infection, reports of neurologic affection keep increasing. Clinical presentation of COVID-19 neurological affliction include myelitis amid many others. Transverse myelitis (TM) can occur in association with this infection, presenting both as postinfectious and parainfectious. Case reports have been published dating back to April, 2020.
Methods: 31-year-old patient with chronic use of benzodiazepines, no other known pathologies, presents with an acute urinary retention, 24 hours later he develops paraplegia. 2 weeks prior, the patient had suffered from anosmia, cough and fever; a RT-PCR SARS-CoV-2 nasopharyngeal swab test is obtained and results positive. Neurological examination documents areflexia and loss of motor strength in lower extremities, with a foley catheter already placed and a clear T10 sensitive level. The patient is hospitalized with the tentative diagnosis of TM following the case definition from the Transverse Myelitis Consortium Working Group and receives infructuous treatment with methylprednisolone followed by gamma globulin.
Results: Completing the diagnostic studies and discarding other inflammatory, infectious and compressive causes, a diagnosis of probable SARS-Cov-2 TM is reached.

Lumbar Puncture	27 leucocytes, 79% lymphocytes, 48 erythrocytes, glucose 54, DHL < 25 and 84 microproteins Culture negative for bacteria and fungi Non reactive VDRL Epstein Barr, Cytomegalovirus, adenovirus, virus herpes simplex virus 1 and 2, varicella zoster, enterovirus, parechovirus, herpes virus 6 and 7, parvovirus B19 negative Oligoclonal bands: negative
Vitamin B12	Normal
Auto-Antibodies	Antinuclear antibodies, antineutrophil cytoplasmic antibodies negative, anti-aquaporin 4 antibodies negative
Acute Phase Reactants	Normal D-Dimer, Reactive C Protein not elevated, Procalcitonin not elevated
Serologies	Negative for HIV and Hepatitis A, B and C
Computerized Tomography	Normal
Magnetic Resonance Imaging	T12 hypertense lesion in STIR and T2 sequencies, with gadolinium enhancement in T1.

Blood Tests and Imaging Studies performed to the patient

Conclusion: Medical experience in the many and varied possible clinical presentations of COVID-19 infection is constantly growing, and more is constantly being discovered concerning the neurological involvement in this infection. Here a case of spinal inflammation -transverse myelitis- is presented in probable association with the virus.
Disclosure: Nothing to disclose.

EPO-530

Predictors of self-reported impact of COVID-19 pandemic among patients with multiple sclerosis

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[1] Department of Neurology, Lisbon, Portugal, [2] Lisbon, Portugal

Background and aims: COVID-19 disease has quickly evolved into a full-scale pandemic. Little is known about the predictors of the impact of COVID-19 pandemic in multiple sclerosis (MS) patients' lives.
Methods: A cross-sectional study using an online survey was conducted from 21st December 2020 through 3rd January 2021. Patients with MS followed-up at Egas Moniz Hospital (Lisbon) were invited to participate. We assed participants self-reported impact of COVID-19 pandemic in their lives. The effect of the demographic, clinical and psychosocial factors was analyzed through univariable and, when applicable, multivariable analysis.
Results: We obtained 256 valid responses (response rate 81%). The median age of the participants was 45 years [18–77] and most of them were females (187, 73.0%). Overall, 205 (80.1%) patients reported that COVID-19 has had a substantial impact in their lives – extreme (40, 15.6%) or high (165, 64.5%). In the univariate analysis, greater impact from COVID-19 was associated with female gender($p=0.011$), age ($p=0.026$), being professionally active($p<0.010$), having more concerns about the pandemic ($p<0.001$), reporting a higher perceived risk to get a future COVID-19 infection ($p=0.002$) and a possible severe infection ($p=0.008$). The multivariate regression analysis revealed that factors predicting greater impact from COVID-19 were age <45 years (OR 2,409; CI95% 1.112–5.220; $p=0.026$), being professionally active (OR 2.374 CI95% 1.139–4.947; $p=0.021$) and having more concerns about the pandemic (OR 17.928 CI95% 7.020–45.790; $p<0.001$).
Conclusion: Younger and professionally active MS patients are suffering from COVID-19 pandemic. Although they could be at lower risk of severe infection, doctors should be aware of their concerns.
Disclosure: Nothing to disclose.

EPO-531

NeuroCOVID protocol and pilot results: a multicentre case-control study of acute stroke and SARS-CoV-2 infection

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Background and aims: Coronavirus disease (COVID-19) can predispose to vascular and neurological complications, through inflammatory and thrombogenic mechanisms. There is a high incidence of stroke and of COVID-19 in Brazil, making it important we better understand the association between stroke and SARS-CoV-2 infection. In view of this, we set up a NeuroCOVID study.

Methods: This prospective case-control study is recruiting across 12 healthcare centres across all five Brazilian regions. We will enroll 1,000 stroke cases and 1,800 inpatients with other nonvascular acute diseases as controls with a 1:2 ratio. The main outcome is acute stroke (ischemic, haemorrhagic, venous thrombosis). The exposure is SARS-COV-2 infection: previous (positive IgG), subacute (positive IgA) or acute (virus detected in nasopharynx). The Protect Code Stroke Protocol was translated into Portuguese to be validated in our population. All participants will respond to standardized questionnaires and have blood and nasopharyngeal swab samples collected at baseline, after signing the consent form (ethics approval nº CAAE36538320.9.0000.5190).

Results: Our pilot study ran at Hospital da Restauração (Northeast Brazil), from the 11th to 31st of December and included 20 cases (mean age 59 years; 50% female) and 14 controls (mean age 52 years; 36% female). Four patients had asymptomatic acute SARS-CoV-2 infection, all of them in the case group (20%).

Conclusion: These preliminary results support our hypothesis of an association between SARS-CoV-2 and acute stroke in Brazil. The final report of the NeuroCOVID study will provide definitive evidence, along with similar studies worldwide.

Disclosure: Yes.

EPO-532

Post COVID-19 myelitis presenting as Partial Brown-Sequard syndrome

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Background and aims: Although rare, myelitis as neurological complications of SARS-CoV2 infection are increasingly recognized.

Methods: We describe a patient with post COVID-19 myelitis presenting as Partial Brown-Sequard syndrome.

Results: A 33-year-old man presented to the hospital with a one-week history of progressive weakness and diminished sensation of the lower limbs. Six weeks before, the patient was diagnosed with SARS-CoV-2 infection, with mild symptoms, from which he fully recovered (at the time negative). Neurological examination revealed right leg motor weakness (grade 4/5), left-sided hemihypoesthesia (T5-T6) and a hyperesthesic zone at T4 on the right. Spinal cord MRI revealed an intra-medullary lesion extending from T3 to T4, at the right anterolateral region, with gadolinium enhancement. Brain MRI was normal. Routine blood tests were unremarkable/negative, including serologies, autoimmune-panel and antibodies anti-MOG/anti-aquaporin 4. Cerebrospinal fluid study was normal, oligoclonal bands were negative and SARS-CoV-2 was not detected by PCR, but serology for SARS-CoV-2 (IgG) was positive. The patient started methylprednisolone (1g/daily for five days) with improvement of the symptoms being discharged on an oral steroids tapering regimen. One month later, the patient was asymptomatic, neurological exam was normal and there was a considerably lesion reduction and no gadolinium enhancement.

Conclusion: We assumed the diagnosis of post-infectious myelitis after COVID-19, considering the delayed temporal profile, no other causes were found after extensive workup and the marked improvement with steroids. A direct infection of the CNS by SARS-Cov2 seems unlikely since the myelitis occurred six weeks after the acute infection and CSF was negative for the virus.

Disclosure: The authors declare no conflict of interest.

EPO-533

COVID-19 anxiety disorders: Psychological and biochemical aspects

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Background and aims: The relationship of psychological factors with general medical indicators, as well as with the possibilities of rehabilitation after an illness, has been analyzed

Methods: The study involved 66 patients, mean age 61 The indices of CRP, the level of ferritin, D-dimer, the level of saturation with the indices of psychological tests were compared. Psychodiagnostic techniques: Metode d'Induction Motivationelle, Impact of Event Scale (IES), Resilience Inventory-Self (RIS), The Fear of COVID-19, Scale Peritraumatic Distress Index (CPDI).

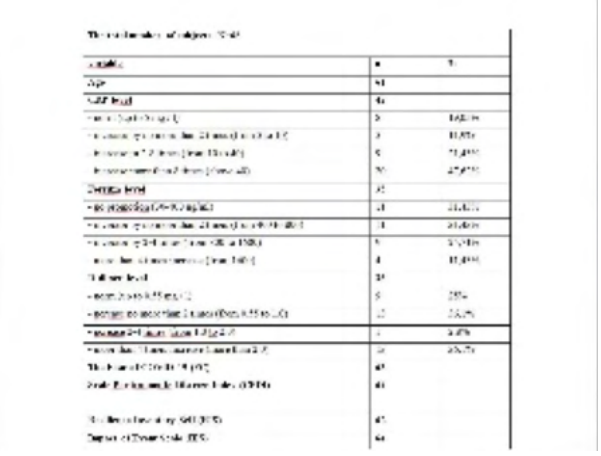

Table 1. Description of the sample

Results: The age of the patients does not correlate with the level of CRP, ferritin and D-dimer, as well as with the scores on the The Fear of COVID-19, CPDI, Resilience Inventory-Self (RIS) and Impact of Event Scale (IES) questionnaires; In the format of an interdisciplinary study, a direct relationship was revealed between the absolute values of ferritin and scores on the Resilience Inventory-Self (RIS) scale (rp=0.363, p<0.05).

Table 2a. Values of the correlation coefficients Rs between medical and psychological indicators in absolute values

Table 2b. Values of the correlation coefficients Rs between medical and psychological standardized indicators

Conclusion: The patient's age does not determine the severity of the cytokine storm and inadequate physiological response to the coronavirus. Ferritin level turned out to be a marker of high resilience (psychological resistance to stress) of the patient according to the study.

Disclosure: Nothing to disclose.

EPO-534

Ogilvie's syndrome in a Patient with Parkinson's Disease and COVID-19 Disease

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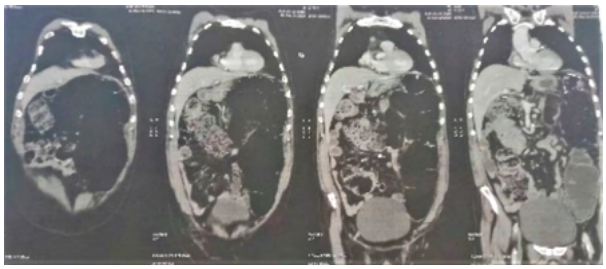
Background and aims: Ogilvie's syndrome or Acute Colonic Pseudo-obstruction (ACP) is a rare condition that presents with colorectal distension in the absence of any mechanical obstruction. Unrecognized and untreated, it may lead to bowel perforation and ischemia. We report a case of ACP in a patient with Parkinson's disease (PD) and COVID-19 disease.

Methods: A 78-year-old male with an eight-year history of PD, hypertension, diabetes and recent diagnosis of Covid19 (~2 weeks prior), presented with a one-month history of abdominal pain, distension and constipation. His exam was significant for a distended and tympanitic abdomen without peritoneal signs. X-rays showed colonic distention with predominant aerocoly at the left colic angle without any identifiable organic obstacle. Labs revealed mild hypokalemia. Presentation was thought to be consistent with ACP. Initial treatment included stopping anti-PD drugs and electrolyte repletion. A trial of atropine failed to relieve the obstruction and resulted in transient bradycardia while colonoscopic decompression was successful and showed no underlying mucosal lesion.



X-rays showed colonic distention with predominant aerocoly at the left colic angle

Results: ACP can be related to multiple etiologies such as diseases of centra l autonomic and enteric nervous systems (PD), or metabolic diseases (Diabetes Mellitus) and can be idiopathic in 5.5%of the cases. It is well established that electrolyte imbalances and certain medications including antiparkinsonians especially Levodopa, calcium blockers decrease gastrointestinal tract motility and may contribute to ACP.

Conclusion: Our case highlights the importance of recognizing ACP in PD patients and fast initiation of symptomatic treatment in order to prevent catastrophic complications. The exact pathophysiology and cause of ACP remain unresolved.

Disclosure: Nothing to disclose.

EPO-535

Recurrent thrombotic event in a young patient with MTFHR mutation and corona virus

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Background and aims: Here, we report a patient with severe acute respiratory syndrome related to coronavirus-2 (SARS-CoV-2) who presented with acute ischemic stroke and later developed nonarthritic anterior ischemic optic neuropathy (NAION).

Methods: Patient data were obtained from medical records from the University Hospital "Firoozgar", Tehran, Iran.

Results: : A 39-year-old man without any significant past medical history initially presented with left hemiplegia and dysarthria after 10 days prodrome of malaise, headache, fever and cough. The oropharyngeal swab test for coronavirus disease 2019 (COVID-19) by qualitative real-time reverse-transcriptase-polymerase-chain-reaction (RT-PCR) assay was positive. One month later he developed an acute painless right eye vision loss with fundoscopic findings consistent with NAION. Digital subtraction angiography (DSA) revealed complete occlusion of the proximal right internal carotid artery (ICA). Trans-esophageal echocardiography showed aortic arch large thrombus. He was found to carry homozygous Methylenetetrahydrofolate reductase (MTHFR) A1298C mutation.

Conclusion: : Our case highlights the rare occurrence of ischemic stroke along with NAION during the COVID-2 pandemic in a previously healthy young man. We hypothesize that the hypercoagulable state related to COVID-19 exacerbated the underlying hereditary thrombophilia due to MTHFR gene mutation.

Disclosure: COVID-19, Large vessel occlusion, AION, Ischemic stroke, Young stroke

Motor neurone diseases 1

EPO-536

Amyotrophic lateral sclerosis: clinical and epidemiological aspects in a Tunisian population

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Background and aims: Amyotrophic Lateral Sclerosis (ALS) is a rare neurodegenerative disorder affecting peripheral and central motor neurons.
Methods: A retrospective and descriptive study over a period of nine years (2010–2019) in the Department of Neurology of CHU Habib Bourguiba, Sfax, including all patients followed for ALS. Neurological examination data, electroneuromyogram (ENMG) and brain and spinal cord MRI data were collected. Prognostic factors were also determined.
Results: We included 47 patients with a mean age of 53.09 years (30 to 82 years). Sex ratio was 2.35 (33H/14F). Median age of onset was 55 years. Three patients presented with familial ALS. The first manifestation was bulbar signs in seven cases, weakness of the upper or lower limbs for the others. The ENMG confirmed the involvement of the peripheral motor neuron. The evolution was marked by rapid worsening in 20 patients, 80% of whom had bulbar signs and most of them were old on onset. The mean age of our patients was lower than the age described in some studies (60 years). The familial form, found in three patients, represents 5 to 10% of cases. Like in the literature data, the spinal form was the most frequent in our serie. The advanced age of onset, bulbar forms and delayed diagnosis were a poor prognosis.
Conclusion: ALS is a serious illness. The evaluation of the various clinical and electrical parameters is essential for both diagnosis and prognosis.
Disclosure: No commercial or institutional support.

EPO-537

A double-blind, placebo-controlled, 6 months clinical trial of curcumin supplementation in amyotrophic lateral sclrosis

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Background and aims: Amyotrophic lateral sclerosis (ALS) is a multifactorial disease in which genetic and environmental factors contribute to its pathogenesis for which oxidative stress plays a key role. Curcumin, known for its neuroprotective capacity, could improve pathological conditions, such as ALS. Aim of the study was to determine whether curcumin oral supplementation (1500 mg/day) could be effective in ALS.
Methods: ALS patients were randomized to receive curcumin (Curcumin Group, CG, n=11) or placebo (Placebo Group, PG, n=11). ALS-functional rating scale, medical research council, body mass index, and oxidative stress biomarkers, including oxidative protein products (AOPPs), ferric reducing ability (FRAP), total thiols (t-SH), were evaluated before (T0), after 3-(T1) and 6-(T2) months of curcumin/placebo treatment. Inter-group (CG>PG) and intra-group (CG or PG) evaluations were carried out.
Results: No change was observed in the clinical parameters after curcumin administration. AOPPs increased in PG at T1>T0 ($p<0.05$), but not in CG. In CG, than in PG, FRAP increased at T1 and at T2 ($p<0.01$), as well as t-SH levels were increased at T1>T0 ($p<0.05$), with a positive trend after six months of curcumin administration (T2>T0, $p=0.05$). In CG compared to PG higher FRAP and t-SH levels were observed at T1 and T2 ($0.01<p<0.001$), while AOPP levels not changed between groups.
Conclusion: Treatment with curcumin shows encouraging results as modulator of the non-enzymatic antioxidants although it not influence the clinical course of the disease. Although further studies are needed to confirm these data, these observations can be useful to deepen knowledge into the pathogenic mechanisms of ALS.
Disclosure: Nothing to disclose.

EPO-538

1-year follow-up of an Israeli cohort with SMA undergoing nusinersen treatment

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Background and aims: Spinal muscular atrophy (SMA) is caused by homozygous disruption of survival motor neuron 1 (SMN1) gene and deficient functional SMN protein. SMA phenotypes may range from severe fatal disease in infancy to minor adult-onset muscle weakness. Nusinersen, an antisense-oligonucleotide that enhances the functional SMN protein expression, was the first drug approved for SMA. This study aimed to examine the outcomes in patients who completed at least one year of treatment.
Methods: We included in a retrospective cohort study data on all the patients diagnosed with SMA who were treated with nusinersen at the SMA multidisciplinary clinic between 2017 and 2019. Demographic and genetic data were collected at baseline. Clinical data were collected before, and one year after starting nusinersen.
Results: 44 patients with SMA type I, II, and III were included in the study (age 0–30 years; 22 with type 1). There was improvement in motor function and specific motor achievements in surviving type I patients (n=20). Earlier treatment initiation (5 months of age) led to better motor functions. A significant decrease in the mean number of hospitalizations was noted ($p<0.008$). Respiratory function and number of gastrostomy procedures remained stable during follow-up. SMA type II patients (n=13) showed no significant improvement. In type III patients (n=9), only motor function improved. In about 25% of our cohort, parental carrier diagnosis was missed due to cis configuration.
Conclusion: Early initiation of nusinersen treatment led to better outcomes and improved morbidity. Newborn screening for SMA is advisable.
Disclosure: AFV and LS served as invited speakers and received research grants from Biogen.

EPO-539

ALS-A Multisystem disorder

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Background and aims: Recent studies widely demonstrate the multisystem involvement of amyotrophic lateral sclerosis. Pathology case studies as well as imaging studies are proving above mentioned. We investigated the clinical features of ALS patients, who appealed to The First University Clinic of Tbilisi State Medical University to define ALS-Plus syndromes.
Methods: Overall 42 patients with ALS were investigated, among them 20 male (47.6%), 22 female (52.3%) , aged 21–84, we documented atypical clinical manifestations of those patients. Brain MRI and electrophysiological studies were done in all patients. The patient survey was taken using Mayo Clinic Laboratories-Neurology patient form, Cognitive changes assessed by Addenbrooke Cognitive Examination scale (ACE III), and Hamilton Anxiety and Depression Scale used for evaluating anxiety severity. Statistics performed by SPSS-11.0.
Results: ALS-Plus syndrome was found in 12 (28.5%) patients , demonstrating extrapyramidal disorders – six (14.2%), autonomic functioning disturbances –10 (23.8%), GI system was mainly affected. Cognitive impairment revealed in 11 patients (26.1%) evaluated with ACE III, among them seven patients fulfilled Neary criteria for FTD. All patients demonstrated mild to moderate anxiety levels. Neurovisualisation revealed more cortical atrophy in ALS-Plus patients in comparison to typical ALS ($p<0.01$). No different electrophysiological patterns were observed in those subgroups.
Conclusion: Results of the present research demonstrate strong evidence of ALS being a multisystem disorder, implying that ALS-plus neurological symptoms should be screened vigorously and managed appropriately.
Testing the patients for possible genetic mutations for the development of ALS-Plus syndrome is needed.
Disclosure: Nothing to disclose.

EPO-540

Kinematic analysis of repetitive finger movements in patients with amyotrophic lateral sclerosis

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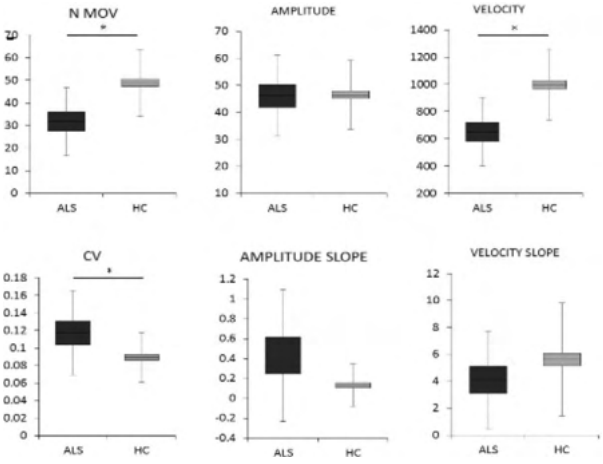
Background and aims: Amyotrophic lateral sclerosis is primarily characterized by the degeneration of motor neurons, leading to muscle weakness and motor impairment. There are some clinical reports of bradykinesia in this condition, but no studies have objectively assessed voluntary movements in these patients. The relationship between motor neurons involvement and movement abnormalities is also unknown. We here kinematically assessed repetitive finger movements in patients with amyotrophic lateral sclerosis as compared to healthy controls. We investigated possible relationships between altered movement kinematics and neurophysiological measures of motor neurons involvement in patients.

Methods: 13 amyotrophic lateral sclerosis patients and 79 healthy controls were enrolled. Finger tapping was assessed by a motion analysis system. Patients also underwent a motor nerve conduction study, a central motor conduction time assessment, and a needle electromyography. Kinematic data from the two groups were compared by non-parametric tests. Possible relationships between clinical, kinematic and neurophysiological data were assessed in patients.

Results: Patients performed fewer movements and they were slower than healthy controls. Patients also showed an altered movement rhythm. The number of movements and the velocity peak correlated with the finger strength and with the amplitude of the compound muscle action potential recorded from the muscles involved in the task. Finally, movement slowness correlated with the denervation activity in the first dorsal interosseus.



Kinematic variables of finger tapping in patients with amyotrophic lateral sclerosis – ALS (dark grey) and in healthy controls – HCs (light grey).

Conclusion: This study provides new information on the evidence of bradykinesia in amyotrophic lateral sclerosis, indicating movement slowness and altered movement rhythm without decrement. In amyotrophic lateral sclerosis movement slowness likely depends on the lower motor neurons involvement.

Disclosure: Nothing to disclose.

EPO-541

Real experience of long-term treatment of late-onset SMA (2/3) with Nusinersen. Madrid, n=24.

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Background and aims: To review the results of the long term treatment of all SMA type 2-3 patients in late childhood to adulthood in the region of Madrid.
Methods: Spinraza® at the approved intrathecal doses and periods. Lumbar punctures done with conscious analgesia (nitrose oxide 50%) either in the examination room or in outpatients operating room. Assessment were done with physical neurological exam, muscular MRC scale, motor scales (CHOP INTEND, HMSE, rULM), respiratory FVC and FEV1, disability EK2 scale and PROs.
Results: 24 cases were treated, eight cases SMA-2 (non-sitters or sitters at start), and 16 cases SMA-3 (non-sitters, sitters or walkers). Ages at start 2,7–74 y. Follow up 10–31 months (median 24). Treated with 6–11 infusions (median 9). In three cases (SMA-2) an Ommaya cervical/occipital reservoir was placed because impossibility to lumbar access, getting an easy and fast access with no complications. Improvement in objective scales were observed in 65% and 50% of cases respectively in upper limb (UL) and lower limb (LL) function. Subjective improvement in strength in 85% and 70% of cases (UL and LL respectively). 95% notified reduced fatigue and faster movements. The improvement was progressive, higher in less affected cases, independently of the age. BiPAP could been retired in 2/4 cases. No patient worsen, none abandoned the treatment. No complications due to nusinersen. The procedure was well tolerated with VAS pain scale 2-3/10. Only 10% of post-puncture pain.
Conclusion: Intratecal nusinersen gives a functional benefit in most part of the patients with late onset SMA, even in adult ages.
Disclosure: Prof Pascual has received honorarium from Biogen, Avexis and Roche for advisory and conferences and participated in phase three trials of nusinersen and risdiplam in SMA1.

EPO-542

Epidemiological clinical profile of patients with amyotrophic lateral sclerosis in reference ambulatory in Bahia-Brazil

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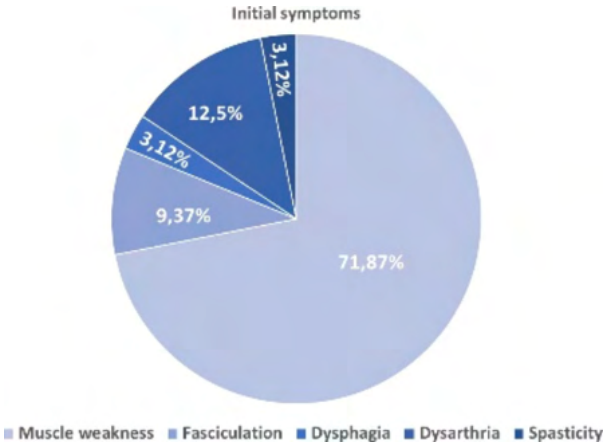
Background and aims: Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disorder, characterized by the degeneration of cortical, bulbar and spinal cord motor neurons, whose main foundation for clinical management is multidisciplinary care.
Methods: The study is a transverse, ambispective and descriptive data, based on information collected through 32 structured interviews, with a non-probabilistic sample selected for convenience of the population of patients with a diagnosis of ALS defined as probable or possible according to the El Escorial Criteria attended at the medical centre of the Escola Bahiana de Medicina from September 2019 to February 2020.
Results: Men constituted 65.62% of the sample, 46.87% declared themselves white, 53.12% have completed high school and 28.12% were rural workers. The mean age at the first symptom of the disease was 50.41 years (±12.41) and the mean age at diagnosis was 58.83 years (± 15.58). 87.5% of patients were classified as defined ALS, 93,75% classical ALS, 84.37% spinal ALS, and 15.62% bulbar ALS, with a predominance of this form in males (60%). Regarding possible risk factors, we highlight a history of traumatic brain injury (21.87%), smoking (21.87%), alcoholism (15.62%), work activity with physical effort (81.25%), vigorous physical activity (23.81%) assessed by the Baecke questionnaire, and others (21.87%).

Demographic characteristics	Frequency (n=32)
Sex	
Female	65,62% (n=21)
Male	4,37% (n=11)
Color	
White	46,87 (n=15)
Brown	37,5% (n=12)
Black	
Scholarity	
Incomplete high school	31,25% (n=10)
Complete 1st degree	6,25% (n=2)
Complete high school	53,12% (n=17)
Higher Education	9,37% (n=3)
Previous occupation	
Rural worker	28,12% (n=9)
Taxi driver/ Driver	18,75% (n=6)
Bricklayer	3,12% (n=1)
Self-employed	15.62% (n=5)
Others	34,37% (n=11)

Demographic characteristics of ALS patients in relation to sex, ethnicity / color, education and occupation prior to the disease

Risk factors	Frequency (n = 32)
Cranioencephalic trauma	
Yes	21,87% (n=7)
No	78,12% (n=25)
Exposure to toxic substances	
Smoking	21,87% (n=7)
Alcoholism	15,62% (n=5)
Pesticides / insecticides	12,5% (n=4)
Solvents	9,37% (n=3)
Family history	
Yes	0% (n=0)
Work activity with physical effort	
Yes	81,25% (n=26)
Light Effort	15,38% (n=4)
Moderate effort	42,31% (n=11)
Vigorous effort	42,31% (n=11)
No	18,75% (n=6)
Physical activity	
Yes	65,62% (n=21)
Vigorous / strenuous	23,81% (n=5)
Moderate	33,33 (n=7)
Light	42,86 (n=9)
No	34,37% (n=11)

Frequency of exposure to potential risk factors associated with ALS



Frequency of initial symptoms of ALS patients

Conclusion: The clinical profile found corroborates previous research, except for the self-declared colour, level of education, age at first symptom and diagnosis, the prevalence of classic ALS and prevalence of bulbar ALS among men.
Disclosure: No conflicts of interest.

EPO-543

Palliative conducts and survival time of patients with amiotrophic lateral sclerosis in ambulatory in Bahia-Brazil

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Background and aims: Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease, characterized by the degeneration of motor cortical, bulbar, and spinal cord neurons, advancing progressively with motor, respiratory and swallowing dysfunction. Therefore, the main foundation for clinical management is multidisciplinary care since there is still no cure for the disease.
Methods: The study was outlined as cross-sectional, ambitious, and descriptive based on information collected through 32 structured interviews, with a non-probabilistic sample selected for the convenience of the population of patients diagnosed with ALS defined as probable or possible according to El Escorial at the medical centre of the Bahiana School of Medicine from September 2019 to February 2020.
Results: Most patients (93.75%) used riluzole; 12.5% underwent gastrostomy, 40.62% used AMBU and 43.75% non-invasive ventilation. The median survival time since the onset of symptoms was 55 (±30.53) months and the median survival time after establishing the diagnosis was 21.27 (±29.22) months. Patients with cognitive impairment accounted for 6.25% and 53.12% showed loss of walking ability. There was no record of deaths.

Medications in use	Frequency (n=32)
Riluzole	93,75% (n=30)
Amitriptyline	31,25% (n=10)
Atropine	9,375% (n=3)
Baclofen	21,875% (n=7)

Frequency of medication use in ALS patients

Palliative conduct	Frequency (n=32)
Gastrostomy	
Yes	12,5% (n=4)
No	87,5% (n=28)
Bag valve mask (AMBU bag)	
Yes	40,62% (n=13)
No	59,375% (n=19)
Non-invasive ventilation	
Yes	43,75% (n=4)
No	56,25% (n=18)

Frequency of gastrostomy, use of bag valve mask and non-invasive ventilation

Possible Outcome	Frequency (n=32)
Presence of cognitive impairment	
Yes	6,25% (n=2)
No	93,75% (n=30)
Loss of gait	
Yes	53,12% (n=17)
No	46,87% (n=15)
Deaths	
Yes	0% (n=0)

Frequency of possible outcomes associated with ALS

Conclusion: The clinical profile found differs from previous studies regarding survival after the onset of symptoms, frequency of cognitive impairment and deaths. The early application of palliative measures, associated with multi-professional care, may be associated with longer survival after the onset of symptoms in patients. Further research is required to greater understand the disease.
Disclosure: No conflicts of interest.

EPO-544

Snake eyes sign in spinal MRI of patients with motoneuron disease (MND): an infradiagnosed sign or a prognosis marker?

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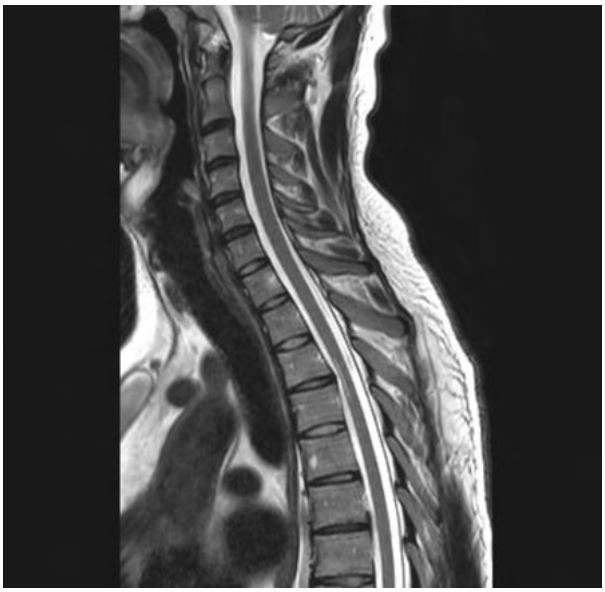
Background and aims: MND is clinically heterogeneous, and nearly 10% of patients with other entities can be incorrectly diagnosed, especially those without upper MN signs. Otherwise, an alternative diagnosis when diffused upper and lower MN signs are present is exceptional.
Methods: A 31-year-old boy without relevant medical, traumatic or family history presented with progressive symmetrical spastic weakness of lower limbs for three months. He didn't have bulbar, sphincter or sensory symptoms. Deep tendon reflexes were brisk. Extensive blood tests, body CT and brain MRI were normal. Spinal MRI showed a symmetrical D2-D3 T1 hypointense and T2 hyperintense signal in the anterior horns with a "snake eyes" appearance, without extradural compression. Cerebrospinal fluid analysis and neurophysiologic examination were normal.
Results: Six months later, he developed left hand weakness, and diffused fasciculations. EMG showed generalized acute denervation signs. Diagnosis of amyotrophic lateral sclerosis (ALS) was made. He is stabilized after three months of follow-up.
Conclusion: The snake eyes sign has been described in cervical spondylosis, Hirayama disease, spinal cord infarction or lower MND. Some reports suggest that it represents a particular lower MND, more common in young men with previous exhausting activity/trauma and better prognosis. In our case there's involvement of upper and lower MN and no relevant antecedents, typical of classic ALS. The MRI finding can traduce the damage to the anterior horn. Evolution will clarify if there's a marker of good prognosis also in classic ALS, or may be an infradiagnosed sign in MND due to technical limitations or absence of axial slices in routine MRI studies.



Longitudinal T2 spinal MRI

Disclosure: Nothing to disclose.

Movement disorders 3

EPO-545

New methods of education in movement disorders for medical students.

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Background and aims: Medical universities in Kyrgyzstan provides an intensive course of neurology discipline in a quiet short time (See Fig.1). Only one session is dedicated to movement disorders. That could be a reason of relatively low knowledge on Parkinson's disease demonstrated by medical students after completion of neurology course during the survey in 2019.

Curriculum	KSMA		KRSU	
	7 term	8 term	7 term	8 term
Seminars	36 h	49h	54 h	36 h
Didactic lectures	14 h	8 h	36 h	18 h
Self education	22 h	9 h	18 h	36 h

Figure 1

Methods: In February 2020 MDPDA has organized an educational course in a new format, including video session and card game for medical students of Kyrgyz State Medical Academy and Kyrgyz Russian Slavic University. The course was in Russian language. The total time was 2 hours. Each participant filled pre- and post course screening of the knowledge on movement disorders.
Results: 28 students participated in the experimental course – 37% men, 63% women, average of 23 years old. 78% of participants competed in the game. 30% of game participants were attendees of each universities' neurology club. 71% of students completed a course of neuroanatomy, syndromology in neurology, 29% fully completed clinical course of neurology. According to results, the average improvement was 19,2%. Complete data is indicated in figures 2 and 3. The highest increase (68.8%) of correct answers was in Q3, while the number of correct answers dropped in only Q2 (12,9%). However, no participant demonstrated a 100% improvement after the session. All students demonstrated high interest and involvement.

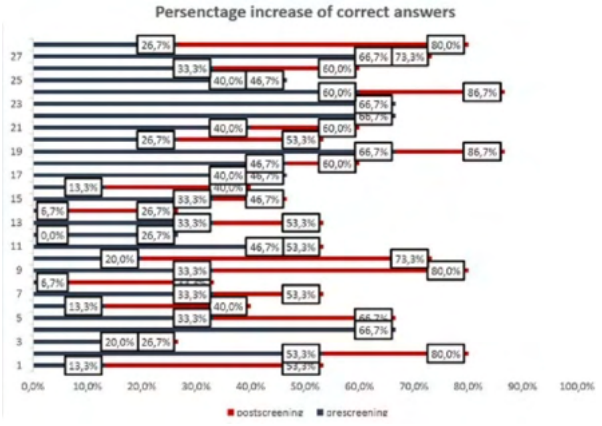

Figure 2

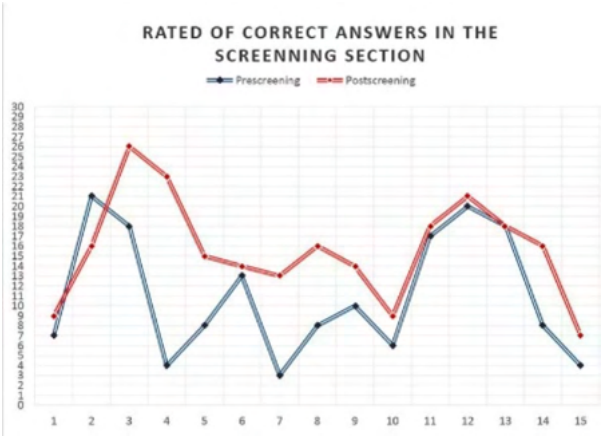

Figure 3

Conclusion: According to knowledge screening results, event of a such format could be considered as a good option to increase the learning effectiveness and interest of students in movement disorders and neuroscience.
Disclosure: The authors declare that they have no competing interests.

EPO-546

A mitochondrial disorder presenting as chorea

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Background and aims: We present the case of a 29-year-old man with progressive generalized chorea involving the orofacial muscles, severe neurosensory deafness and mental retardation.
Methods: The choreatic movements started six years before, after treatment with risperidon due to psychomotor agitation. Later on, the patient developed tetraparesis and lower limb spasticity. His father suffered from cardiomyopathy and diabetes mellitus and died at the age of 55. His mother had cardiomyopathy, thyroidopathy and premature menopause and died at the age of 53. His aunt (from the paternal side) had mental retardation. Brain MRI showed leucoencephalopathy. Nerve conduction studies showed mild sensorimotor polyneuropathy. In view of the patient's phenotype, we performed genetic testing.
Results: Genetic testing with whole exome sequencing revealed two mutations: a homozygous missense mutation c.404G>A (p.Arg135Gln) in the gene MRPS22 located on 3q23 coding the mitochondrial ribosomal protein S22, which causes a combined oxidative phosphorylation deficiency five and a heterozygous non-sense c.847G>T (p.Glu283Ter) mutation in the SLC17A8 gene located on 12q23.1, causing autosomal dominant deafness type-25.
Conclusion: We present a rare case of mitochondrial disorder presenting with chorea. Mutations in the MRPS22 gene have been associated with a wide range of symptoms including developmental delay, microcephaly, dysmorphic features, hypotonia, spastic tetraplegia, cardiomyopathy and ovarian dysgenesis 7. Neuroleptics such as risperidone in mitochondrial disorders can lead to the appearance of chorea or other extrapyramidal syndromes.
Disclosure: The case is also submitted as video case for the basal ganglia club.

EPO-547

Botulinum toxin therapy in control of motor manifestations and anxiety level in patients with craniocervical dystonia

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Background and aims: Nonmotor symptoms are highly prevalent in craniocervical dystonia (CCD) and affect quality of life. Botulinum toxin (BT) is considered the most effective treatment of focal dystonia and has high effectiveness in controlling motor symptoms. The severity of motor symptoms and anxiety level was also analyzed in patients with CCD in appliance with BTA treatment and its regularity.
Methods: The study included 76 patients with CCD divided into three subgroups: A)patients who have never received BTA injections, B)patients regularly receiving the BTA injections (3–4 times a year) and) patients receiving BTA injections less than 2 times a year. Severity of motor manifestations was scored using the Unified Dystonia Rating Scale (UDRS), depression and anxiety level was assessed with Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI).
Results: 26,5% patients had mild anxiety level and 8,4% had severe anxiety. Mean estimated total UDRS score was 11,2±2,6 in group A, 9,2±3,6 in group B and 9,8±3,1 in group C. There was significant difference in UDRS scores in group A and group B (p=0,039). There was no significant difference in anxiety level among these groups. Correlation between the severity of motor manifestations and anxiety level was not found in patients with CCD.
Conclusion: Regular injections of BTA support control of motor manifestations of CCD. Mild and severe anxiety is prevalent in more than one third of patients with CCD and should be considered as important aspect of quality of life.
Disclosure: Nothing to disclose.

EPO-548

Opicapone in Clinical Practice in Parkinson's UK Patients with Motor Fluctuations: Findings from the OPTIPARK Study

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Background and aims: Opicapone (OPC) proved to be effective in treating end-of-dose motor fluctuations in Parkinson's Disease (PD) patients [1,2]. The OPTIPARK study evaluated OPC 50-mg in a heterogeneous population of patients treated in real-world conditions [3].

Methods: OPTIPARK was a prospective, open-label, single-arm, multicentre trial conducted in Germany and the UK. Patients with motor fluctuations received OPC 50-mg in addition to current antiparkinsonian treatment. Primary efficacy endpoint was Clinician's Global Impression of Change (CGI-C) after three months. Secondary efficacy endpoints included Patient's GIC (PGI-C) and Unified Parkinson's Disease Rating Scale (UPDRS).

Safety assessments included evaluation of treatment-emergent adverse events (TEAEs). Here UK-only data is reported.

Results: 132 patients took one OPC dose (Safety Set; Table 1) and 102 completed three months' treatment. Of 128 patients with post-baseline efficacy data (Full Analysis Set), 72.7% and 78.4% experienced any (very much/much/minimal) improvement on CGI-C and PGI-C after three months, respectively (Table 2). There were relevant improvements on UPDRS II and III scores (Table 3). TEAEs considered at least possibly related to OPC were reported for 65.2% of patients, the most frequently reported being dyskinesia (27.3%) and dry mouth (12.1%). 87.8% of TEAEs were of mild or moderate intensity. Serious TEAEs considered at least possibly related to OPC were reported for 2 (1.5%) patients.

Table 1. Baseline characteristics (Safety Set)

Characteristic	N=132
Male gender, n (%)	81 (61.4)
Age, mean (SD) years	67.3 (8.4)
Disease duration, mean (SD) years	8.9 (5.2)
Duration of motor fluctuations, mean (SD) years	2.6 (2.8)

SD, standard deviation

Table 2. CGI-C and PGI-C results after 3 months (Full Analysis Set)

Category	CGI-C N=128	PGI-C N=102
Not assessed	1 (0.8)	0
Very much improved	15 (11.7)	14 (13.7)
Much improved	47 (36.7)	39 (38.2)
Minimally improved	31 (24.2)	27 (26.5)
No change	22 (17.2)	9 (8.8)
Minimally worse	5 (3.9)	10 (9.8)
Much worse	5 (3.9)	1 (1.0)
Very much worse	2 (1.6)	2 (2.0)

CGI-C, Clinician's Global Impression of Change; LOCF, Last Observation Carried Forward; PGI-C, Patient's Global Impression of Change; LOCF applied to CGI-C

Table 3. Changes from baseline in UPDRS scores (Full Analysis Set)

Scale	N	Mean (SD) change from baseline to 3 months	p-value
UPDRS II (activities of daily living) score at OFF stage	101	-2.2 (4.9)	<0.0001
UPDRS II (activities of daily living) score plus III (motor function) score at ON stage	102	-3.7 (10.7)	<0.0001
UPDRS III (motor function) score at ON stage	100	-2.7 (8.3)	<0.0001

SD, standard deviation; UPDRS, Unified Parkinson's Disease Rating Scale; p-values obtained through Student's t-test

Conclusion: OPC 50-mg was effective and generally well tolerated in UK PD patients with motor fluctuations treated in clinical practice.

Disclosure: 1.Ferreira et al., Lancet Neurology 2016;15(2):154-165; 2.Lees et al., JAMA Neurol. 2017;74(2):197-206; 3.Reichmann et al., Transl Neurodegener. 2020;9(1):9

EPO-549

Case report: Adult onset dopa-responsive dystonia

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Background and aims: Dopa-responsive dystonia (DRD) incorporates a group of clinically and genetically heterogeneous disorders related with limb-onset, diurnal fluctuation and sustained response to low-dose levodopa. Mutations in the GCH1 gene are its most common cause. However, next generation sequencing (NGS) techniques allowed the identification of other genetic causes, such as mutations in PRKN gene, which has been classically associated with early-onset Parkinson's disease.
Methods: This poster will be presented as a single case report.
Results: A 33 year old woman, with previous hypertension and dyslipidemia, presented with a 2-year history of lumbar pain episodes associated with involuntary contraction of the lumbosacral musculature causing a right-side truncal deviation. A year later, she reported episodes of left foot stiffness that worsened in the evening. Physical examination revealed right sided torticolis and same side lumbar deviation, with trapezius hypertrophy and gait claudication with left foot abnormal everson. There was no parkinsonism. Brain and spinal cord MRI were normal. The NGS panel for dystonias revealed heterozygous mutations in PRKN and ATP13A2 genes. Patient started levodopa increasing dosage upto 400mg with resolution of axial dystonia and is under evaluation for treatment with botulinum toxin.
Conclusion: Levodopa trial is mandatory for focal dystonias, even when adult-onset. Recent advances in genetic diagnostic techniques will expand our knowledge in hereditary dystonias and probably demonstrate new phenotypes for old genes.
Disclosure: The manuscript has not been published previously and is not under review at any other journal. There is no financial or any other type of conflict of interest related to the manuscript.

EPO-550

Hemichorea and contralateral hemidystonia after acute stroke

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Background and aims: Movement disorders occur uncommonly in association with stroke (1%), despite the frequent involvement of the basal ganglia. Hemichorea/hemibalism and dystonia are the most common.
Methods: Case report of a patient with sudden-onset of right hemichorea with left hemidystonia after an ischemic stroke in the right internal carotid artery (ICA) and left anterior cerebral artery (ACA) territories.
Results: A 58-year-old woman came to the emergency department with left hemiparesis of sudden onset. She had a history of aneurysms in both ICAs treated with flow diverter devices (left ICA two years earlier and right ICA three days before admission). Brain CT-scan was normal, Angio-CT showed occluded right ICA and perfusion-CT showed hypoperfusion of right ICA and left ACA territories. She underwent mechanical thrombectomy with partial recanalization; during the arteriographic procedure a hipoplasic left A1 segment with common origin of both ACAs from right ICA were seen (Figure 1). 21 days after admission she developed irregular involuntary right-sided movements (chorea), dystonia of left limbs and cervical dystonia with torticollis to the right and laterocollis to the left (video). Brain MRI showed right fronto-parietal cortex, caudate and lenticular nucleus and left caudate nucleus restricted diffusion (Figure 2). Diagnosis of right hemichorea with left hemidystonia of vascular origin was made. Clonazepam 0,5mg twice daily was started, with little improvement.

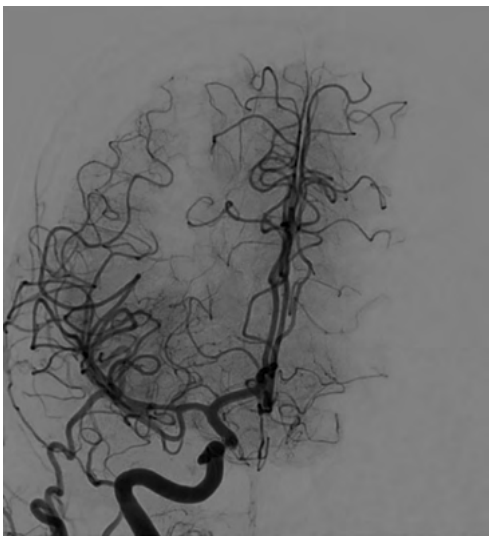

Figure 1. Arteriography: common origin of both ACAs from right ICA

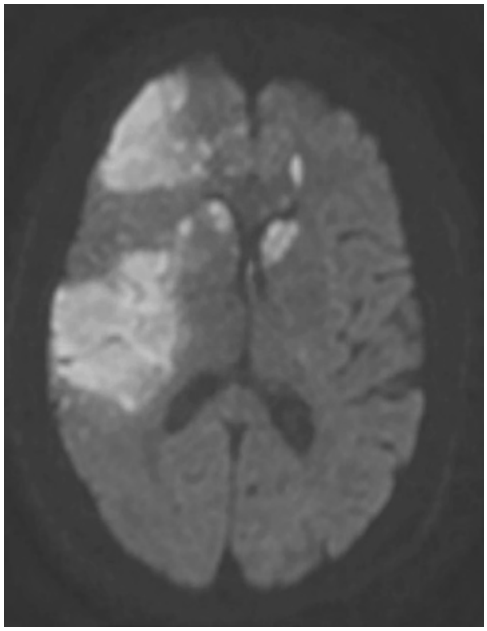

Figure 2. Brain MRI: right fronto-parietal cortex, caudate and lenticular nucleus and left caudate nucleus restricted diffusion

Conclusion: Even though ipsilateral hemichorea and hemidystonia of vascular origin can rarely occur simultaneously, to our knowledge, this is the first reported case of the occurrence of each movement disorder in different body sides following an acute ischemic stroke.
Disclosure: Nothing to disclose.

EPO-551

PHARC syndrome, mimics and chameleons: an illustrated report of the first Portuguese case

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Background and aims: Polyneuropathy, hearing loss, ataxia, retinitis pigmentosa, and cataracts (PHARC) disease is a rare autosomal recessive neurodegenerative condition caused by mutations in the /-hydrolase domain-containing 12 (ABHD12) gene. Less than 40 cases have been reported to date.
Methods: N/A
Results: A 29-year-old female patient with a personal history of bilateral severe hearing loss since age 16 and cataracts with retinitis pigmentosa at age 19 presented to our outpatient clinic with a progressive 10-year-long tremor history on both upper limbs. On examination, there was a bilateral upper limb postural tremor and distal myoclonus, mild proximal tetraparesis, abolition of deep tendon reflexes, loss of pinprick sensation up to the shin and wrists, loss of vibratory sensation on both hands and feet, impaired postural sensation on both feet, mild appendicular ataxia, mild bilateral ptosis and congenital convergent strabismus of the left eye (with no ophtalmoparesis). A brain MRI revealed global moderate cerebral and cerebellar atrophy. Nerve conduction studies and electromyography revealed a demyelination sensorimotor polyneuropathy on both upper and lower limbs. Blood and CSF analyses were unremarkable. Muscular biopsy revealed lipid accumulation within muscle fibers. Genomic sequencing of the ABHD12 gene revealed a homozygotic mutation (c.1054C>T).
Conclusion: The differential diagnosis of hereditary cerebellar ataxias is challenging, with many patients being un- or misdiagnosed. However, an uncommon association of ataxia, retinitis pigmentosa and demyelinating polyneuropathy narrows the diagnostic possibilities. When faced with this picture, the diagnosis of PHARC disease should be considered.
Disclosure: Nothing to disclose.

EPO-552

The Wolfram-like syndrome in a 72-year-old woman

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Background and aims: The Wolfram syndrome is an orphan genetic disease. Most of the patients have the recessive mutation in the Wolfram syndrome gene 1 (WFS1, 4p16.3). Dominant WFS1 gene mutation in connection with variable clinical symptoms is called Wolfram-like syndrome, WFSL. This is a case report of Wolfram-like syndrome (WFSL), which includes hearing loss, optic atrophy, low glucose tolerance, various neurological symptoms.
Methods: A study of a 72-year-old woman, included anamnesis, physical neurological examination, and analysis of instrumental and genetic tests.
Results: The patient complained of the inability to walk due to severe ataxia, apraxia of walking, severe hypotrophy of the leg muscles for four years. Prior to this, the patient had an atactic gait and hunched over when walking for 10 years. Family history: her sister from 45 y. o. had a severe cerebellar ataxia and dementia for 12 years. Their father was blind in both eyes. There were progressive neurologic symptoms: vertical gaze paralysis, hearing loss, pathological postures like cervical dystonia and Pisa syndrome, cerebellar ataxia, peripheral neuropathy, severe dementia, catatonia as a symptom of "air cushion" in the supine position, stereotyped smacking lips, moderate dysphagia, orthostatic hypotension, urinary and fecal incontinence. Brain MRI: cortical and olivopontocerebellar atrophy. DNA sequencing: a previously undescribed heterozygous mutation in exon 8 of the WFS1 gene (chr4: 6303465G> A, rs150465110) was revealed, leading to the appearance of a site of premature translation termination at codon 648 (p. Trp648Ter, NM_006005.3).
Conclusion: This is the case of WFSL with a previously undescribed heterozygous mutation.
Disclosure: Nothing to disclose.

EPO-553

Clinical characteristics of Tremor syndromes in a mexican cohort

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Background and aims: Essential Tremor (ET) is a tremor syndrome of at least three-year history of tremor in the absence of other neurological signs. The term ET-plus was proposed to include those patients with clinical characteristics of ET and additional neurological signs of uncertain relationship. In dystonic tremor (DT), dystonia predominates. Identifying differences between these syndromes may lead to a better approach.
Methods: Observational cross-sectional descriptive study of patients with tremor syndromes who attended the movement disorder clinic from January 2019 to December 2020. Patients were classified by a movement disorders neurologist according to the Consensus Statement on the Classification of Tremors.
Results: 27 patients were included. six (22%) patients were classified as ET, 16 (59%) as ET-plus, and five (18%) as DT. Patients had a mean age of 64, 69 and 63 years, respectively; 34%, 28% and 60% were female, respectively; a positive familiar history was observed in 100%, 42% and 80%, respectively; with disease duration of 18, 17, and 12 years, respectively. Hands were the initial affected area in 100%, 87%, and 0%, respectively. DT initiated with head tremor in 100% of cases. ET-plus symptoms were 62% cervical dystonia, 31% memory impairment or sleep disorders, 25% mood disorders or urinary symptoms. 40% of patients with DT reported instability.
Conclusion: ET presented more frequently in males. ET-plus reported less frequently a family history. The most common sign reported in ET-plus patients was cervical dystonia. DT classically starts in the head, seems to have less disease duration and is rarely accompanied by other neuropsychiatric symptoms.
Disclosure: The authors have declared no potential conflicts of interest.

EPO-554

Clinical determinants that influence a later molecular diagnosis of Huntington's Disease

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Background and aims: Huntington's Disease (HD) is one of the most common monogenic neurological disorders presented in adulthood. Subjects can become symptomatic from childhood to eighties. HD onset phenotypic differences have not been well-characterized in the literature. Factors associated with the onset of molecular diagnosis are scarce. This study aims to identify factors that could delay the time to diagnosis.
Methods: A cross-sectional study with HD molecular patients attending Movement Disorder Clinic at the National Institute of Neurology and Neurosurgery in Mexico City was performed. Major symptom at onset was classified in motor, psychiatric, and mixed, depending on the predominant symptom within the first year of the presentation. A comparative analysis between groups includes demographic and clinical variables as gender, age, CAG-size, family history, age of onset, major symptom at onset, age of molecular diagnosis, and time to diagnosis (defined as the age of clinical onset to age of molecular diagnosis).
Results: A total of 107 patients (50.5% female) with a mean age of 49±12.8 years were included. Median CAG size was 45 (38–73). Mean age of onset was 39±12.9 years. Mean time to diagnosis was 6.4±6.4 years. In the comparative analysis, psychiatric-group had a longer time to diagnosis compared to the motor-group (p=0.02). Novo cases showed a trend to an older onset, but less time to diagnosis, in comparison to familiar cases.
Conclusion: Psychiatric-onset was associated with a later diagnosis. Earlier recognition of the disease could reduce this time, translated into faster treatment, and a future potential improvement in the patients' quality of life.
Disclosure: The authors report no disclosures.

EPO-555

Violent and emotional behaviors in idiopathic RBD predict higher risk of phenoconversion to the overt synucleinopathy

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Background and aims: Abnormal behavioral manifestations in REM sleep are the hallmark of idiopathic REM sleep behavior disorder (iRBD), which is known to be the prodromal stage of alpha-synucleinopathy. The aim of this study was to evaluate whether categorized motor events (ME) are related to the risk of developing phenoconversion.
Methods: 34 iRBD patients (5 women, 29 men; age 67.7±7.2) with a mean follow-up duration 2.9±1.1 years. and 33 controls (10 women, 23 men; age 61.5±8.2) were examined. The ME captured during REM sleep were classified into four categories, previously defined by Frauscher et al., according to clinical severity: minor/simple jerks, major, complex and violent. Association with vocalization and emotional subtext was determined when observed concurrently. Survival analyses were conducted to estimate phenoconversion risk using Kaplan-Meier analysis and using Cox proportional hazards regression adjusted for age and sex.
Results: An average frequency of 110.8±75.2 ME per hour were identified in iRBD, 7.5±11.6 in the controls ($p<0.001$). Of these ME in patients, 68.4% were classified as minor/simple jerks, 9.3% as major, 21.7% as complex and 0.7% as violent. During follow-up seven patients (24.1%) phenoconverted, yielding a yearly phenoconversion rate 8.3%. Association with increased hazard ratio for phenoconversion was found in violent ME frequency (HR=7.1 [1.6–32.1]; p=0.012), total violent ME duration (HR=10.7 [2.3–50.4]; p=0.007), and in frequency of emotional ME (HR=6.1 [1.4–27.6]; p=0.016).
Conclusion: Higher amounts of violent and emotional ME should be considered as a predictor of forthcoming phenoconversion.
Disclosure: Supported by Charles University grant Progres Q27/1LF. Authors have no conflict of interest to disclose.

EPO-556

Non-motor symptoms seasonal variations in patients with Parkinson's disease

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Background and aims: Diurnal fluctuations in Parkinson's disease(PD) are well recognized mainly in relation to motor symptoms. For example, patterns of daily activity differ significantly between patients with Parkinson's disease(PwPD) and healthy elderly people[Daniel J.van Wamelen, 2019]. Our aim was to determine the relationship between seasons and non-motor symptoms(NMS) in PwPD.
Methods: The study included 612 PwPD from the SSMU database. 128 PwPD were examined four times a year for three years (2017–2019) using NMS evaluating scales: MDS-UPDRS, Apathy scale, BDI-II, HADS, ESS, PDSS, SCOPA-AUT, MoCA-test, QUIP-RS, C-SSRS, PDQ-39. first survey was conducted during December-February, second – March-May, third – June-August, forth – September-November. The primary result was a seasonal difference in overall scores on the NMS scales.
Results: The same PwPD from the Department of neurology, SSMU database were examined all four times. There was a seasonal difference in the spectrum and severity of NMS in PwPD: the highest scores in season 1 (winter months) and the lowest in season 3 (summer months). Increased NMS in the off-season were mainly observed in the area of the cardiovascular system and falls ($p=0.021$), hallucinations ($p=0.037$) and perception problems ($p=0.041$), a tendency to drowsiness and fatigue ($p=0.031$). It is noteworthy that indicators of depression that could potentially explain these NMS differences did not change depending on the season in PwPD.
Conclusion: NMS in PD fluctuate throughout the year: symptoms worsening in the winter months compared to the summer months($p<0.05$), which indicates dysfunction of the suprachiasmatic nuclei. This should be taken into account when changing treatment regimens and interpreting the results in clinical trials.
Disclosure: Nothing to disclose.

EPO-557

The influence of impulse-compulsive disorders on depression in patients with Parkinson's disease

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Background and aims: Depression and impulse control disorders(ICDs) are both common in patients with Parkinson s disease(PwPD) and their coexistence is frequent. Our aim was to determine the relationship between depression and ICDs.
Methods: The study involved 360 PwPD (women: men=179:181) accompanied by cognitively intact close person without depression. All patients were examined using the following scales: QUIP-RS, MoCa, BDI-II (major, minor and subthreshold depression were distinguished). After testing on the QUIP-RS scale, relatives were interviewed about the presence of ICDs in PwPD.
Results: Depression was more common in PwPD without ICDs than in patients with them: 73% (146/200) vs. 35% (56/160); $p<0.05$. Individuals with and without ICDs were compared by gender. Among women, no statistically significant difference was found in the mean scores assessing depression between groups – 17 (12;24) and 16 (12;24), $U=1278.5$, $p=0.797$. Among men, a more severe depression was revealed in the group with ICDs – 23 (14;27), in comparison with individuals without ICDs –16 (10;21), $U=531.0$, $p=0.018$. At the same time, a higher score was revealed for the cognitive-affective component of depression in the group of PwPD with ICDs – seven (4;11), without ICDs – 9 (6;13), $U=566.0$, $p=0.040$. There were no statistically significant differences in somato-mental component – 9 (6;11) and 11 (8;13), respectively, $U=605.5$, $p=0.091$. Depression was remarkably more common in male PwPD with gambling – 100%[8/8] vs. 48%[84/173], $p=0.018$; hypersexuality – 92%[24/26] vs. 28%[44/155], $p=0.001$; hobbyism – 86%[33/38] vs. 24%[35/143], $p=0.001$.
Conclusion: Depression is associated with and precedes ICDs in PwPD. Depressed male PwPD are more likely to experience gambling, hypersexuality, and hobbyism.
Disclosure: Nothing to disclose.

EPO-558

The impact of medication reviews involving pharmacists on people with Parkinson's disease: a systematic review (SR).

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Background and aims: Inappropriate polypharmacy and complicated drug regimens are common in people with Parkinson's disease (PwP). In PwP, drug-related problems may have deleterious effects on clinical outcomes and wellbeing. The use of the medication review, a structured evaluation of patients' pharmacotherapy, where drug-related problems are detected and corrected, could be an effective tool to support positive clinical outcomes and minimise adverse outcomes.
Methods: The primary aim of this SR was to evaluate the effectiveness of the medication review involving pharmacists (MRP), on the quality of life (QoL) in PwP. The secondary aim was to assess the impact of MRP on motor and non-motor symptoms of Parkinson's disease (PD). Randomised controlled and quasi controlled trials were included as identified in electronic searches conducted in AMED, CINAHL, Embase and MEDLINE databases. The inclusion criteria were studies with a population of PwP, MRP as intervention, reported in English and with QoL or PD symptoms as outcomes.
Results: There were 3,647 studies from the original search. seven were selected for full text review; five met the inclusion criteria. The results were mixed. four out of five selected studies found significant improvement in QoL. Of the two selected studies that reported the impact of MRP on PD symptoms, one found improvement in motor symptoms while the other did not, and vice versa for non-motor symptoms.
Conclusion: MRP generally improved QoL in PwP. There was insufficient evidence to conclude that MRP improved motor or non-motor PD symptoms. Further controlled studies are required to confirm these results.
Disclosure: Nothing to disclose.

Neurogenetics 1

EPO-559

Elevation of circulating MiR-206 in transportinopathy, capainopathy, sarcoglycanopathy limb girdle dystrophy.

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Background and aims: We analyzed mutations,, disease progression of eleven LGMD patients, investigated MiR-206 , a myomiRNA with important function in skeletal muscle development,regeneration and degeneration.
Methods: We followed eleven patients affected by various subtypes of LGMD-D2((transportinopathy); LGMD-R1(calpainopathy), LGMD-R3-R5 (sarcoglycanopathy).We studied the circulating miR-206 in serum by qRT-,PCR,, muscle MRI was done with 1.5 Tesla apparatus.
Results: The severe evolution of disease type is associated with the expression levels of miR-206, which was significantly elevated in our LGMD patient series.In particular, we observed an over-expression of miR-206 that was 50–80 folds elevated in two patients with a severe and early disease course in the transportinopathy and calpainopathy sub-types.
Conclusion: The functional impairment was observed clinically and muscle loss and atrophy documented by muscle MRI. This study provides the first evidence that miR-206 is associated with phenotypic expression and it could be used as a prognostic indicator of LGMD disease progression.
Disclosure: This study was supported by AFM Grant 22392.

EPO-560

Differentiating CSF1R-related adult-onset leukoencephalopathy and CADASIL, two cases from Hungary

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Background and aims: Cerebral arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is a well-known genetic small vessel disease, associating with migraine, strokes, white matter lesions, and cognitive impairment. CSF1R-related adult-onset leukoencephalopathy with axonal spheroids and pigmented glia (ALSP) in contrast is a more recently characterized leukodystrophy with overlapping symptoms with CADASIL.
Methods: We performed next generation sequencing panel for adult-onset leukodystrophies in patients with leukodystrophy, and selected patients whose samples were submitted to our center for CADASIL sequencing in Hungary. Neurologic examination and 3T MRI was performed at all patients.
Results: We identified a female patient with a heterozygous CSF1R likely pathogenic rare variant [(NM_005211.3): c.1771G>A (p.Gly591Arg)] in the leukodystrophy group and a female patient with the same variant in the CADASIL group. The first patient was investigated for early onset dementia, with a family history consistent with autosomal dominant inheritance. Brain MRI showed frontal predominant demyelination, and brainstem involvement. The second patient was examined for headaches (consistent with migraine with aura), which occured from age 12 years and associated with white matter lesions. Neurologic examination was normal. The brain MRI showed focal-confluating T2 hyperintensities around the ventricles and deep border zones. We present the clinical-genetic and imaging characteristics of the two patients.
Conclusion: CADASIL and ALSP might resemble each other. In our cases, the same CSF1R variant caused a typical clinical picture consistent with ALSP, and an atypical picture resembling the early stage of CADASIL. In this presentation, we highlight the importance of the genetic stratification of the leukoencephalopathies.
Disclosure: Supported by the Hungarian Brain Research Program KTIA_NAP_2017-1.2.1-NKP-2017-00002.

EPO-561

A familial slowly progressing early-onset dementia caused by the rare 7-OPRI mutation in the PRNP gene

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Background and aims: Creutzfeldt-Jakob disease is the most common of the five known human prion diseases, causing various neuropsychiatric symptoms, myoclonus, cerebellar, corticospinal, extrapyramidal manifestations with rapid progression. While sporadic CJD accounts for approximately 90% of the cases, mutations in the PRNP gene can cause familial prion disease.
Methods: In this report we review the case of two young brothers with a rare mutation in the PRNP gene, causing slow progression CJD.
Results: A 29 year old patient's early onset personality change, coordination problems, aphasia, and cognitive decline started at age 24. He had positive family history, as his 31 year-old brother showed signs of cognitive deterioration, and his father also developed similar symptoms when he was 38, and passed away 10 years later. Neurological examination detected cerebellar ataxia and severe dementia with a MMSE score of 12/30. Brain MRI showed medium grade, diffuse cerebral atrophy. EEG found diffuse subcortical, dominantly thalamocortical dysfunction without prion specific alterations. Sequencing the PSEN1, PSEN2, APP and MAPT genes did not detect alterations. A heterozygous 168 bp octanucleotide insertion (7-octapeptide repeat insertion) in PRNP was identified in the brothers. On follow-up, at the age of 31, the patient requires constant care, and his dementia progressed severely (MMSE 0/30). His brother lost his job but still able to take care of himself.
Conclusion: In the differential diagnosis of the early onset dementias, prion disorders always have to be excluded, especially when classic monogenic dementias are already ruled out. The 7-OPRI mutations may result in a wide variety of clinical phenotypes.
Disclosure: Nothing to disclose.

EPO-562

Abstract withdrawn

EPO-563

A new variant in OPA1 linding to ADOA-plus disorder

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Background and aims: OPA1 mutations are associated to autosomal dominant optic atrophy (ADOA). We present the case of a woman at first evaluated for hyperckemia and myalgias, in which a new heterozygous variant of the OPA1 gene was identified.
Methods: The patient's clinical history was collected and radiological, bioptical, neurophysiological and gene investigations were performed.
Results: From the clinical history emerged that the patient had been diagnosed with Hashimoto's thyroiditis and Sjogren's syndrome, and for years she had suffered from hearing loss, visual impairment and migraine. The neurological physical examination did not reveal any noteworthy sings, but short stature, thinness, diffuse muscular hypotrophy were noticed. Muscle biopsy showed central hyporeactivity of fibers to oxidative reactions, muscle MRI was normal and brain MRI revealed numerous subcortical confluent gliotic hyperintense areas in T2 sequences. Optic nerve conduction studied with the visual evoked potentials showed a remarkable bilateral increase of the peak latency of the main component of about 20 msec; the study of the visual field revealed a deficit in the lateral sectors and the ophthalmological evaluation reported pale optic disc. A new heterozygous variant c.830 T>C (p. Leu277Pro) in exon 8 of OPA1 gene was found at screen analysis and it is classified as of uncertain significance in VarSome.
Conclusion: OPA1 is an ubiquiteusly expressed dynamin-related GTPase, wich play an imporant role in mitochondrial fusion and in maintaining inner mitochondrial membrane integrity. The new OPA1 variant here described and the multi-systemic involvement of the case, make the mutation plausible to cause an ADOA-plus disorder.
Disclosure: Nothing to disclose.

EPO-564

Comprehensive electrophysiological analysis of SCN1A Arg1596Cys mutation in a family with evolving epilepsy phenotypes.

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Background and aims: Epileptic syndromes caused by mutations of the SCN1A gene, encoding a subunit of the voltage-gated Na+ ion channel (Nav1.1), are heterogeneous/phenotypically different disorders. The variability of phenotypes due to particular mutations allows to hypothesize about the involvement of additional factors, modifying the phenotype resulting from dysfunction of Nav1.1.

Methods: The family, showing epilepsy phenotype evolution from GTCS+ to DRVT due to SCN1A mutation was investigated. Mutation was identified by Sanger sequencing, rearrangements were excluded by MLPA. WES was performed in mutation carriers for comparative analysis of channel coding genes. The Nav1.1 dysfunction was analysed in vitro by voltage-clamp methodology. An effect on the clinical neurophysiological level was investigated by the nerve excitability study (NES) performed in mutation carriers.

Results: Substitution of the Nav1.1 p.Arg1596Cys was identified in five family members (3 generations) – presenting GEFS+, DRVT and no symptoms. NES performed for four symptomatic subjects showed significantly lower rheobase with almost equal strength-duration time constant and significantly shorter relative refractory period in comparison to control group. The patch clamp study showed changes in sodium channel's activation and steady-state inactivation properties. WES analysis, showed presence of the additional CACNA1H variant only in DRVT patient.

Conclusion: Now, when personalized therapy is around the corner the goal of diagnostic should be not only identification of the causative mutation but establish its functional consequences. In the case of SCN1A however we should draw our attention to the fact that not all pathogenic variants are responsible for severe phenotype, even identified in DRVT patients.

Disclosure: Work financed by funds of Polish National Science Centre, grant 2015/17/B/NZ4/0266.

EPO-565

Methylation status of MAPT gene in patients with Parkinson disease in Russian population

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Background and aims: The pathogenesis of Parkinson disease (PD) involves genetic and environmental factors. The relationship between environment and changes in gene expression can be explained by epigenetic mechanisms, particularly, DNA methylation. We have chosen MAPT gene to study DNA methylation because H1 haplotype and some polymorphisms in MAPT gene increase the risk of PD.

Methods: We studied 40 PD patients (mean age 57.86 years, 18 males, 22 females). We analyzed DNA methylation level by performing bisulfate sequence analysis of untranslated exon 0 of MAPT gene containing 19 CpG-sites near 5'-end of the CpG-island. In each sample and in each CpG site we calculated a percent of methylation, (C/C+T)*100. The haplotypes were identified by exon 14 sequencing and determination of haplotype-linked polymorphism (rs1052553). The same analysis was also performed in healthy age- and sex-matched control samples (n=26).

Results: In total, 10 of 19 CpG-sites showed hypermethylation in PD cases in comparison with the control group ($p<0.05$). In PD patients two of 19 CpG-sites had significantly higher methylation level in H1 haplotype carriers in comparison with patients carrying H2 haplotype ($p<0.05$). There were no significant correlations with clinical findings, such as the age of patients, age at onset, duration of the disease, gender, family history, form and stage of the disease, and treatment with L-dopa.

Conclusion: This is the first data on MAPT gene methylation status in PD patients in Russian population. We suggest that MAPT could play a role in the pathogenesis of PD, and the level of methylation could be associated with genetic variants.

Disclosure: The study was supported by RSF grant #17-75-20211.

EPO-566

Description of two families with two new mutations in familial cerebral cavernous malformations genes

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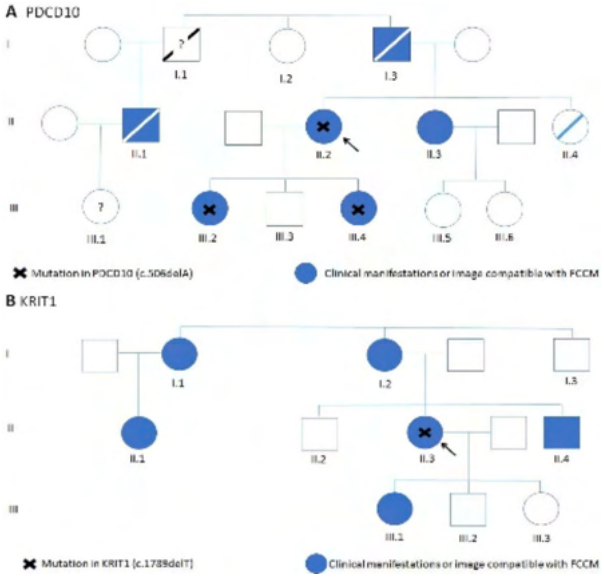
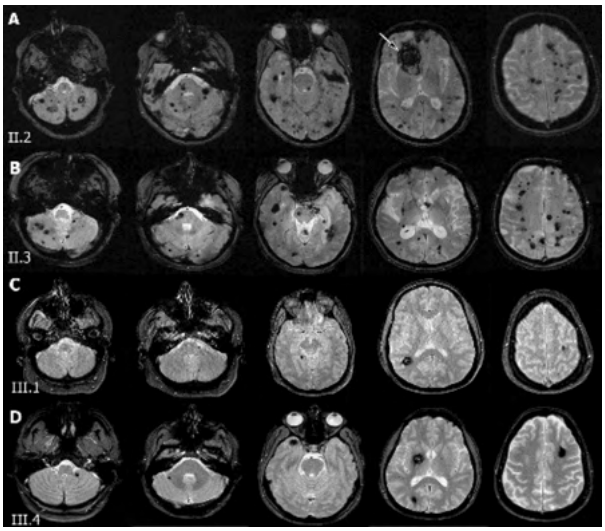
Background and aims: Cerebral Cavernous Malformations (CCM) are dilated aberrant leaky capillaries presented in the Central Nervous System. Familial CCM is an autosomal dominant inherited condition related to mutations in KRIT1, Malcavernin or PDCD10.
Methods: Clinical history revision, genetic studies and MRI were performed.



The patients with clinical manifestations or image compatible with Familial Cerebral Cavernous Malformations (FCCM) are in blue. A cross select patients where the genetic study was positive while the arrows point the proband in each family.

Results: Here, we show two unrelated families presenting familial CCM due to two non-previously described mutations in KRIT1 and PDCD10 which respectively produce a truncated protein. Clinical phenotype was highly variable among carriers from asymptomatic individuals to others presenting diplopia, seizures or severe intracranial hemorrhage. PDCD10 patients showed a more aggressive course and they also associated with presence of multiple meningioma.

Next Generation Sequencing and Sanger Sequencing showing the mutations found in PDCD10 (A) and KRIT1 (B).



Fast-Field Echo (FFE) sequence showing chronic bleedings in relation to CCMs. Patients II.2 and II.3 show more abundant lesions than III.1 and III.4. Moreover, in II.2 a right frontal intracranial hemorrhage is identified (arrow).

Conclusion: This work support previous findings regarding familial CCM and provide evidences for the pathogenicity of two new mutations in CCM genes.
Disclosure: Nothing to disclose.

Neuroimmunology 1

EPO-567

Anti-SOX1 encephalitis manifesting as progressive supranuclear palsy-like syndrome

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Background and aims: We present a case report with rapidly progressive supranuclear palsy (PSP)-like syndrome associated with anti-Sry-like high mobility group box (SOX) 1 antibodies.
Methods: A 69-year-old man presented with a two-year clinical history of progressive asymmetric akineto-rigid syndrome, vertical ophthalmoplegia, postural instability with falls, dysphagia, behavioral changes, and left upper limb dystonia. Magnetic resonance imaging (MRI) of the brain showed moderate midbrain atrophy. Dopamine transporter (DaT)-scan revealed right striatal dopaminergic denervation. Contrast-enhanced thoraco-abdomal-pelvic computed tomography (CT) showed the absence of occult neoplasm. Cerebrospinal fluid (CSF) revealed mild hyperproteinorrachia (86mg/dL) and mild pleocytosis (5 leucocytes/mm^3), in the absence of oligoclonal bands. Anti-SOX1 antibodies were detected in the serum (but absent in CSF), in the absence of other neural surface and intracellular autoantibodies. Treatment with intravenous cyclophosphamide (1g/m^2/month for six months) and plasma exchange showed poor clinical response.
Results: Anti-SOX1 antibodies, strongly related to underlying malignancy (especially small-cell lung cancer), are associated with the involvement of the peripheral (e.g. Lambert-Eaton myasthenic syndrome, polyneuropathy) and central (e.g. limbic encephalitis, cerebellar degeneration syndromes) nervous system. To the best of our knowledge, this is the first case of PSP-like syndrome related to anti-SOX1 antibodies encephalopathy.
Conclusion: Autoimmune encephalitis associated with anti-SOX1 antibodies has to be taken into consideration in the presence of rapidly progressive atypical parkinsonism with PSP-like syndrome.
Disclosure: Nothing to disclose.

EPO-568

Morvan syndrome. Lights and shadows of a rare disease. Case report

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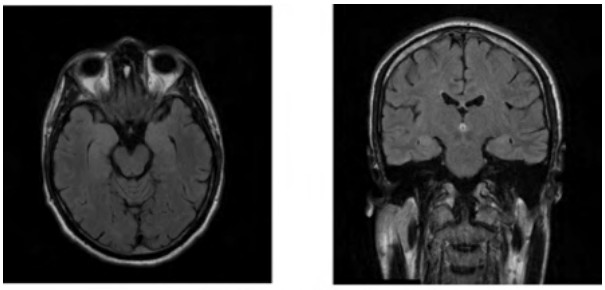
Background and aims: Initially named "chorée fibrillaire", Morvan syndrome (MS) is characterized by three clinical keys: peripheral hyperexcitability, autonomic instability and encephalopathy. Its prevalence is rare, about 100 cases have been described in the medical literature. In 1998 its relationship with anti-potassium channel antibodies was described. Here we present a case report and review the literature, highlighting the importance of clinical suspicion.
Methods: A 48-year-old man presented during the past three months, pleuritic pain, insomnia, visual hallucinations, dysautonomia (difficulty in urination, dysthermia, piloerection, profuse sweating, arterial hypertension, sinus tachycardia) and generalized myokymias. A mediastinal mass was found, although its study was inconclusive. Cerebral MRI, EMG and lumbar puncture were performed, giving a clue about the diagnostic orientation.
Results: As a diagnosis we consider an inflammatory encephalitis, with clinical suspicion of MS, and started corticosteroid therapy since admission. The MRI showed loss of sulcus delimitation and increased symmetric FLAIR signal in the medial temporal region, EMG put in evidence abundant myokymias. Due to lack of clinical improvement, we start intravenous immunoglobulins, although the treatment was stopped due to the patient's hemodynamic instability that led him to death in the third day of treatment. We obtained post-mortem positivity for anti-potassium channel antibodies (anti-CASPR2 and anti-LGI1), confirming the suspected diagnosis of MS.



MRI T2 FLAIR axial and coronal

Conclusion: Having in mind the three clinical diagnostic keys it's important to consider MS in the differential diagnosis. Due to its clinical heterogenicity, strict monitoring of dysautonomia is necessary, and empirical treatment should be considered when the diagnosis is suspected.
Disclosure: Nothing to disclose.

EPO-569

Motor stereotypy in anti NMDAR encephalitis

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Background and aims: Anti NMDAR encephalitis presents with wide range of movement disorders and is an important cause of secondary stereotypy. Motor stereotypy in NMDARE is under reported.
Methods: Retrospective analysis of 10 antibody proven NMDARE patients admitted to our department between July2017 and June2020.
Results: Age varied between 2.5 and 32 years.90% were females. All patients had encephalopathy and 50% had seizures. Movement disorders were seen in 90% cases. Chorea (60%,), dystonia (50%) and motor stereotypy (50%) were the predominant movement disorders. Out of the five cases with stereotypy three had simple and two had complex motor stereotypy Motor stereotypy was associated with chorea in 40% cases ,with dystonia in 40% cases and 20% had all these three. A child of 2,5years presented with autistic regression with hand stereotypy. Hand stereotypy was seen in 80% and one patient had stereotyped whole body movements. MRI Brain was normal in all patients with stereotypy. None of patients with stereotypy had ovarian lesions.
Conclusion: NMDARE presents with polysymptomatic movement abnormalities. Motor stereotypy is a common movement disorder in NMDARE and is overlooked, Motor stereotypy may differentiate NMDARE from other autoimmune encephalitis.
Disclosure: Nothing to disclose.

EPO-570

The clinical spectrum of neurological disorders associated with GAD antibodies: a case series

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Background and aims: Glutamic acid decarboxylase (GAD) antibodies (Abs) have been associated with several neurological disorders such as stiff-person syndrome (SPS) and temporal lobe epilepsy (TLE). Herein, we describe our two-year case series of three patients with their clinical spectrum and correlate it with available evidence.
Methods: Revision of our hospitalization database between January 1st 2019 and January 1st 2021. Identification and description of three patients with neurological disorders associated with GAD Abs. Review of literature and discussion with our results.
Results: Patient 1 was a 64-year-old female who developed limbic encephalitis with TLE. Patient 2 was a 46-year-old female with type-1 diabetes mellitus who suffered a stiff-leg syndrome. Patient 3 was a 66-year-old male with active poorly-differentiated squamous cell tonsil and lung carcinoma, who developed acute motor sensory axonal neuropathy associated with anti-GM3 antibodies and, eight days later, TLE. All of our patients had titers of GAD-65 Abs>2,000U/mL in cerebrospinal fluid and responded to immune therapy consisting on methylprednisolone and intravenous immunoglobulin. Due to a relapse three months later, patient 1 required maintenance treatment with mycophenolate mofetil with no new relapses in a five-month follow-up control. Patient 3 died because of a pneumonia on day +11 since hospitalization.

	Patient 1	Patient 2	Patient 3
Gender, age (years)	Female, 64	Female, 46	Male, 66
Relevant medical history	Hemolytic anemia Endometrioid carcinoma G1 FIGO 1a: H + BSO (2016)	T1DM	Synchronous SCC of lung (cT4N3M0, Stage IIIC) and tonsil (cT1N2cM0, Stage IV): CTX*-RT (2020)
Neurological syndromes	Limbic encephalitis and temporal lobe epilepsy	Stiff leg syndrome Ophthalmoparesis and multidirectional nystagmus	Temporal lobe epilepsy AMSAN (anti-GM3)
Oligoclonal bands in CSF	NA	+	NA
GAD-65 Ab titers in CSF (U/ml) with RIA	>2.000	>2.000	>2.000
Other relevant studies	Brain MRI: normal Body 18F-FDG PET/CT: negative for tumor; high uptake in inferior TLs (mainly left) EEG: fast sharp activity in both TLs (mainly left)	Brain and column MRI: normal Body CT: negative EMG: no CMUA	Brain and column MRI: normal EEG: fast sharp activity in left TL
Immune therapy received	MP 5 g IVIG 2g/kg	MP 5g IVIG 2g/kg	IVIG 2g/kg
Outcome	1 relapse (month +3) with good response to MMF	No relapses	Death (pneumonia, day + 11)

*CTX received: carboplatin plus paclitaxel

Abbreviations: Ab: antibody AMSAN = Acute Motor Sensory Axonal Neuropathy; CMUA = continuous motor unit activity; CSF = cerebrospinal fluid; CTX-RT = chemoradiation; EEG = electroencephalogram; EMG = electromyogram; H + BSO = hysterectomy and bilateral salpingo-oophorectomy; IVIG = intravenous immunoglobulin; MMF = mycophenolate mofetil; MP = methylprednisolone; NA = not available; RIA = radioimmunoassay; SCC = squamous cell carcinoma; TL = temporal lobe; T1DM = type 1 diabetes mellitus

Conclusion: Our case series supports the high heterogeneity of neurological syndromes associated with GAD Abs. Although no criteria exist to establish a pathogenic link between them, it is crucial to report and properly discuss all possible associations since the complete neurological spectrum is yet to be determined.
Disclosure: Nothing to disclose.

EPO-571

Autoimmune Encephalitis – Which Cognitive and Functional Outcomes?

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Background and aims: Prognosis in Autoimmune Encephalitis (AE) remains poorly defined. We aimed to assess functional and cognitive status of subjects with AE followed at a Portuguese tertiary center.

Methods: Retrospective analysis of clinical data on subjects with clinically definite AE followed at a Portuguese tertiary center from Jan-2009 to Dec-2020.

Results: 10 patients were enrolled, six (60%) with antibodies to N-methyl-D-aspartate receptor (NMDAR) and four (40%) to leucine-rich glioma-inactivated protein 1 (LGI1). One NMDAR patient had a late relapse. The Modified Rankin Scale (mRS) score before onset was zero for all patients. Median mRS at nadir was four (IQR 2–5). Dysautonomia and epileptic status occurred in six (60%) and three (30%) patients, respectively. Five patients (50%) required mechanical ventilation and tracheostomy. The median delay from onset to immunotherapy was 35 days (IQR 20–119). All subjects received ,line immunotherapy, six (60%) needed escalation, and three (30%) were kept on maintenance therapy. On follow-up [median time from treatment three months (IQR 2–4.5)], nine patients (90%) were independent (mRS<3). Eight patients underwent neuropsychological evaluation [median time from treatment 10 months (IQR 6.25–14.00)]. Five patients (62.5%) presented mild cognitive impairment, 66% (n=3) with normal or improving cerebral magnetic resonance imaging. One patient had a probable contribution from Human Immunodeficiency Virus (HIV). Another patient didn't undergo neuropsychological evaluation due to severe cognitive deficits.

Conclusion: In accordance with the literature, our sample presented high levels of motor independence despite meaningful cognitive impairment, at short time follow-up. Such cross-sectional analysis ought to be extended to uncover patients' hurdles in daily life.

Disclosure: Nothing to disclose.

EPO-572

Effects of nicotine in primary culture of neural cells and protective action against aminochrome neurotoxicity

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Background and aims: Parkinson's disease (PD) is a neurodegenerative disorder characterized by loss of dopaminergic neurons. Studies have suggested that some cellular and molecular disorders induced by aminochrome, a molecule derived from dopamine, are involved in the neurodegeneration. On the other hand, studies have shown that nicotine protects neural cells against aminochrome cytotoxicity. This study aimed to evaluate the effect of nicotine on neuroprotection and glial cell response in in vitro model of PD induced by aminochrome.

Methods: Primary microglia cultures were obtained from neonatal Wistar rats (0–2 days) cortex and mesencephalic primary cultures were obtained from Wistar rats embryos (15–16 days) (CEUA Protocol 127A/2017). The primary cultures were treated with 25 μM aminochrome and/ or nicotine (0.01 or 1 μM) for 48 h and analyzed by propidium iodide and Rosenfeld's staining.

Results: It was observed that 0.01 μM and 0.1 μM nicotine prevented the cell damage induced by aminochrome and induced cellular vacuolization. It was also observed that treatment with 0.01 μM nicotine induced morphological changes characterized by increased branching in microglia.

Conclusion: The results found in the present study demonstrate that nicotine protects neural cells against aminochrome cytotoxic in primary culture. Further studies are needed to characterize its mechanism of action.

Disclosure: Support: FAPESB, CAPES and CNPQ.

EPO-573

Kappa index in patients with autoimmune encephalitis

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Background and aims: The diagnosis of autoimmune encephalitis (AE) can be complex and is supported by the presence of inflammatory changes in the cerebrospinal fluid (CSF), including intrathecal immunoglobulin synthesis (IS). Aim was to calculate the kappa index (CSF/serum kappa free light chain-KFLC-divided by CSF/serum albumin ratio), as a marker of IS, in patients with a diagnosis of AE or possible AE according to the Graus criteria.
Methods: CSF/serum KFLC were tested using Freelite kits (The Binding Site Group, UK) on samples stored after the diagnostic spinal tap of patients with AE/possible AE between 2009 and 2019.
Results: We included 31 patients: 22 with AE (7 anti-LGI1, six anti-NMDAR, two anti-CASPR2, two anti-GAD, two anti-Ma2, 1 anti-VGKC, 1 anti-GABAbR-positive and one antibody-negative) and nine with possible AE. Eight AE (36%) and one possible AE patient (11%) had CSF-restricted oligoclonal bands (OCB) and three patients each in the AE (14%) and possible AE group (33%) had pleocytosis (>5 cells mm3). Kappa index had a mean value of 9.1 (±13.3) in AE and 0.6 (±1.2) in possible AE patients. Among AE patients, it was highest in anti-NMDAR (12.6±19.5) and lowest in anti-LGI1 encephalitis (0.87±1.6). Kappa index was three in 13 (59%) AE and in one (11%) possible AE patient. In two AE patients (9%) an elevated kappa index was the only abnormal CSF inflammatory marker.
Conclusion: If confirmed in other large series, kappa index might integrate OCB and pleocytosis as a supportive biomarker of neuroinflammation among the Graus criteria.
Disclosure: DF has received travel funding and speaker honoraria from The Binding Site Group (Birmingham, UK) and support to her institution through the supply of Freelitekits for research purposes.

EPO-574

Lateral temporal lesion in anti-LGI1 autoimmune encephalitis

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Background and aims: The clinical presentation of anti-LGI1 autoimmune encephalitis typically includes epileptic seizures, memory impairment, faciobrachial dystonic seizures, and hyponatremia. It is frequently associated with a temporomesial lesion, and immunotherapy improves its prognosis.
Methods: A 37 year-old male presented with a three-month history of progressive short-term memory impairment, and several sudden and short shiver-like episodes, along with a fearful feeling, sometimes triggered by sound stimuli. Additionally, he referred multiple and short episodes of forced involuntary movements of his left hemiface and upper limb, sometimes triggered by intense emotions. He also had left complex auditory hallucinations. Past medical history was unremarkable, except for migraine with visual aura.
Results: Neurological examination disclosed anterograde and retrograde amnesia, and left faciobrachial dystonic seizures. Blood work documented a hypoosmolar hyponatremia. Brain MRI showed one large right lateral temporal lesion, and a small left frontal lesion, both hyperintense in T2/FLAIR. Anti-LGI1 antibody was positive in the CSF. EEG did not show epileptiform activity. Antiepileptic medication alone did not improve symptoms. After five days of methylprednisolone and five days of IV immunoglobulin, symptoms improved substantially.
Conclusion: The presence of memory impairment and possible emotional epileptic seizures suggest limbic encephalitis diagnosis; particularly anti-LGI1, due to the faciobrachial dystonic seizures and hyponatremia. However, a lateral temporal lesion was documented (instead of the typical temporomesial location), causing auditory focal epileptic seizures. In anti-LGI1 encephalitis, the involvement of other temporal regions is rare, and usually found simultaneously with temporomesial lesions. Lateral temporal involvement has not been previously described, expanding clinical and imaging presentations.
Disclosure: Authors have no conflicts of interest.

EPO-575

Cyclophosphamide treatment in Neuromyelitis Optica Spectrum Disorder

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Background and aims: The objective of paper was to evaluate the efficacy of early treatment of cyclophosphamide in NMOSD patients. Cyclophosphamide is widely used for NMOSD patients, while a consensus of timing to receive cyclophosphamid has not been proposed.
Methods: We conducted a retrospective review of NMOSD patients based on medical records. Included patients were divided into three groups: group intravenous phamide, group cyclopho-sphamide after intravenous metilprednizolon , group intravenous metilprednizolon. Time to next relapse was adopted as the endpoint.
Results: Patients from group intravenous metilprednizolon+cyclophosphamide had a longer duration of remission compared with patients from group cyclophosphamide after intravenous metilprednizolon (p=0.025) and group intravenous metilprednizolon (p=0.000), and longer duration showed in the group cyclophosphamide after intravenous metilprednizolon when compared with group intravenous metilprednizolon (p=0.005). We found that older age of initial attack was a risk factor for NMOSD patients (HR 1.235; p=0.022), and younger age of receiving treatment was a protect factor (HR:0.804; p=0.023). Partial patients have used cyclophosphamide before this study in group intravenous metilprednizolon+cyclophosphamide, result showed there was no significance between the patients who had or had not used cyclophosphamide (p=0.299).
Conclusion: Cyclophosphamide could prolong the duration of remission after treatment, especially given within two weeks after attack. Patients who received cyclophosphamide combined with glucocorticoids had a preferable effect than glucocorticoids alone in the remission.
Disclosure: No support was received for this study.

EPO-576

Anti- Ma2 encephalitis and its many disguises. Pearls and pitfalls in the diagnosis of autoimmune encephalithis.

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Background and aims: Anti-Ma2 encephalitis is a paraneoplastic syndrome manifesting as limbic encephalitis (LE) or as diencephalic or brainstem dysfunction. Diagnosis consists of typical MRI findings and presence of anti- Ma2 antibodies in the serum and cerebrospinal fluid. The symptoms are usually subacute and they precede the neoplasm diagnosis.This work describes a patient with atypical symptoms and course of autoimmune encephali /1/2014–10/1/2019) who were treated for PACNS. The subjects with secondary causes for vasculitis were excluded.
Results: We identified nine patients (7 female, two male), resulting in an estimated incidence of 1.62/1,000,000. Their mean age was 50.6 (36–59) years. Five (55.6%) had mild pleocytosis and elevated proteins in their CSF. All had typical findings on MRI, with positive angiography in six (66.7%) patients. However, no biopsy was performed. All were treated with corticosteroids and cyclophosphamide (CYC), the latter being introduced in 19.9 (7–29) days after admission. Mean treatment time with CYC was 13.2 (11–16) months, switching it to mycophenolate mofetil (MMF) (66.7%) or azathioprine (AZA) (33.3%). All patients benefited from treatment in form of no relapses. Patients' NIHSS mean values at discharge and after six months were 3.88 (0–10) and two.44 (0–11).
Conclusion: The results are comparable to those in the literature. Our experience proves to be relatively safe to treat patients with CYC for 12 months, switching it to MMF/AZA with low risk for relapses, especially in patients with low initial NIHSS score.
Disclosure: Nothing to disclose.

EPO-578

Gfap astrocytopathy: coexisting anti nmdar and anti gfap antibodies in a case of autoimmune encephalitis

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Background and aims: Glial fibrillary acidic protein (GFAP) is an intracellular intermediate filament expressed in astrocytes. Human GFAP astrocytopathy was first described in 2016. Only a few case reports and case series exist to date and further information on clinical disease course and diagnostic investigations are needed.
Methods: We describe a case of a young woman who presented with headaches and autonomic dysfunction. Clinical progress, extensive investigation and outcome are described.
Results: A 38-year-old woman presented with an episode suspected as aseptic meningitis followed by rapid deterioration with autonomic dysfunction, hallucinations, delusional disorder, a´d cognitive and sleep disturbances. The laboratory and imaging studies demonstrated CSF pleocytosis with positive oligoclonal bands. Brain MRI was normal. EEG demonstrated generalized slowing, without epileptiform discharges. CSF and serum autoimmune panels detected anti NMDA and anti GFAP antibodies. Total body CT found teratoma in her left ovary. Diagnosis of autoimmune encephalitis triggered by an occult teratoma was made. The teratoma was removed and high dose intravenous corticosteroids followed by IVIG treatment resulted in marked clinical improvement.
Conclusion: Information on the novel diagnosis of GFAP astrocytopathy remains scarce and requires further studies. Data is essential on the various clinical courses, exact pathological mechanisms, as well as diagnostic work-up, treatment and overlapping autoimmune syndromes such as exemplifies in our case. The coexisting of NMDAR+GFAP antibodies in the CSF increases the probability of finding a teratoma and emphasize the need for a through investigation.
Disclosure: Nothing to disclose.

Neurological manifestation of systemic diseases 1

EPO-579

Third nerve palsy and diffuse large b cell lymphoma: case report and literature review

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Background and aims: Isolated oculomotor nerve palsy occurs exceptionally in patients with diffuse large B-cell lymphoma (DLBCL). Typical radiologic findings include third nerve and cavernous sinus enhancement. We describe a patient with oculomotor nerve palsy secondary to lymphomatous infiltration and normal brain MRI.
Methods: Case report and literature review.
Results: A 83 year-old woman with poorly controlled hypertension, presented with left periorbital pain and binocular diplopia. Neurological examination revealed slow left pupil reaction to light, left ptosis and left sided incomplete external oculomotor nerve palsy. She had a past history of DLBCL that was treated with six cycles of chemotherapy according to the R-CHOP scheme, with complete remission for 10 months. Gadolinium-enhanced MRI showed no abnormal findings. The lumbar puncture revealed pleocytosis. On flow cytometry 10% of neoplastic B-cells were detected, therefore intrathecal chemotherapy was initiated. We conducted a literature review and found 12 detailed case reports of similar clinical presentation: 58% were male, the left eye was predominantly affected (75%), 25% presented periorbital pain and in 50% pupils were involved. CSF study was perfored in 58% of the cases and only two patients revealed a normal MRI. Oculomotor nerve mononeuropathy was the initial manifestation of lymphoma in five patients.
Conclusion: In our case, despite normal MRI and inadequately controlled hypertension which could point towards an ischaemic mechanism, CSF study confirmed lymphoma's relapse. Even though isolated third nerve palsy in DLBCL is rare, a normal MRI does not exclude a lymphomatous process and a lumbar puncture should strongly be considered.
Disclosure: We declare no disclosures.

EPO-580

Putting the focus on Neurolupus: a clinicalchallenge. Case report

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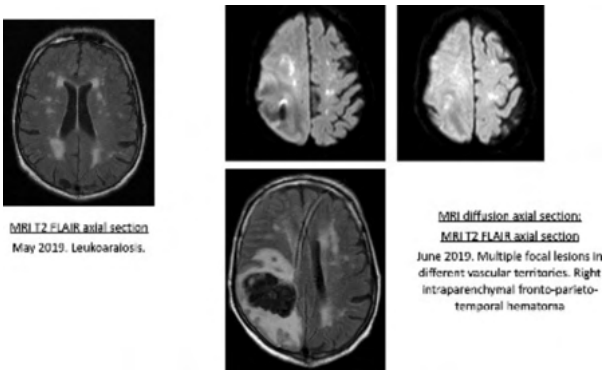
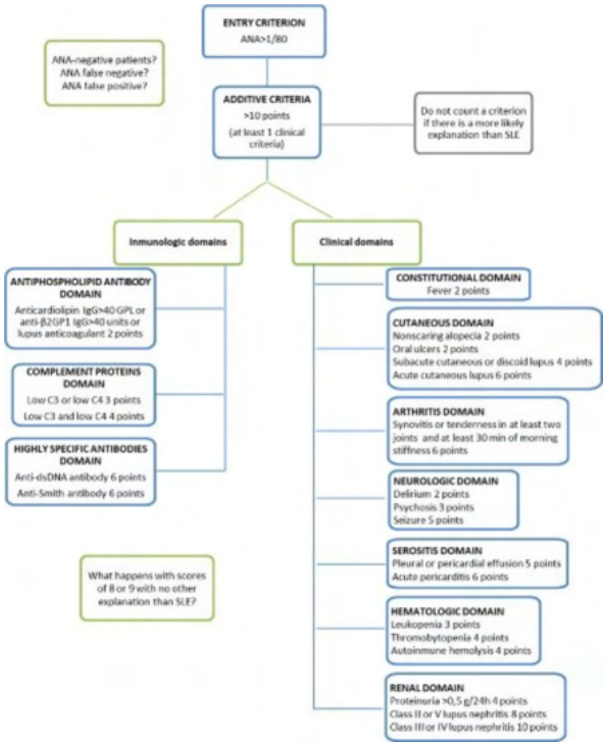
Background and aims: Systemic lupus erythematosus (SLE) is an autoimmune disease which can practically affect any organ of the body, neurologic symptoms occur in 10–80% of patients. In the absence of SLE diagnostic criteria, SLE classification criteria are often used in clinical practice as guidance when making the diagnosis. Recently, new criteria have been developed by the European League Against Rheumatism (EULAR) and the American College of Rheumatology (ACR). In this case report, we pretend to discuss its utility in clinical practice.
Methods: We present a 76-year-old man with a history of multiple ischemic strokes of undetermined etiology with current symptoms of left facio-brachio-crural hemiparesis and hemihypoesthesia and sudden severe visual deficit with a NIHSS score of 20. A head CT scan put in evidence a right fronto-parieto-temporal hematoma. A blood test showed VSG 121mm*, lymphopenia 900*, ANA 1,280*, anti-dsDNA 40IU/ml*, anti-Sm (-), lupus anticoagulant (+), anti2-glycoprotein 8, anticardiolipin (-), anti-Ro 1375 UC*, anti-La 757*, normal levels of complement and Coombs hemolytic anemia (+).



Results: As a diagnosis we consider a possible SLE with CNS involvement (EULAR/ACR 14 points) and started corticosteroid therapy, hydroxychloroquine and mycophenolate with spectacular clinical response, improving from a NIHSS of 20 to 7.



Conclusion: In the event of hematomas or cerebral ischemias with unknown cause or in patients without cardiovascular risk factors, it is important to consider Neurolupus as a differential diagnosis, since it can improve the patient's prognosis. Since neurolupus represents a diagnostic challenge, in selected patients who meet classification criteria, empirically immunosuppressive treatment could be interesting.

Disclosure: No disclosures.

EPO-581

A case report of a patient with neurological symptoms and ACTH producing tumor

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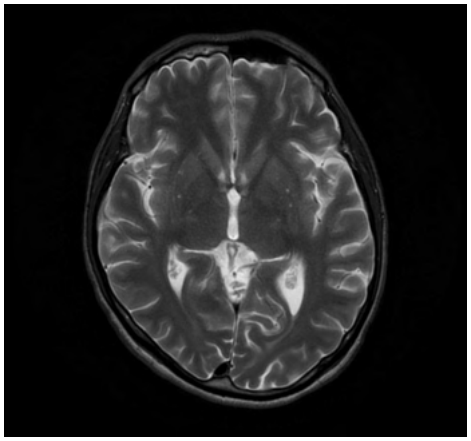
Background and aims: Ectopic adrenocorticotropic hormone (ACTH) secretion typically results from an occult, slow-growing tumor. The diagnosis of these relatively small tumors can be difficult especially when it presents with neurological disorders.

Methods: Somatic and neurological status, laboratory tests, computed tomography scan (CT),magnetic resonance imaging(RI).

Results: We present a clinical case of a 43-year-old man with complaints of nausea,vomiting and fever,changed behavior. The patient was initially hospitalized in the department of psychiatry. Due to the suspicion of organic delusional disorder, he was admitted in the department of neurology with meningoradicular irritation syndrome, cognitive impairment,astheno-adynamic and paranoid syndrome. The patient was with severe hyponatremia (105mmol/l), increased C-reactive protein and ferritin, negative hepatitis B and C, RPR, HIV, COVID19, X-ray on thorax. Central nervous system infection was ruled out by examination of cerebrospinal fluid and performed MRI of the brain (1). Improvement of his condition was observed when steroid treatment was started. The hyponatremia was still persisting so ACTH and cortisol levels were checked and Addison disease was observed. Treatment with methylprednisolone and fludrocortisone was started. Because of the severe weight reduction a CTscan of the abdomen was performed with suspicion for hepatic secondary lesion and stomach cancer (exclude with fibrogastroscopy) (2). The patient was checked for tumor markers because hyponatremia persist. Due to high levels of carcinoembryonic antigen and neuron-specific enolase, CT of the chest was performed. It showed carcinoma of the right lung (3). The patient was diagnosed with ACTH-producing low-grade bronchial adenocarcinoma after biopsy.



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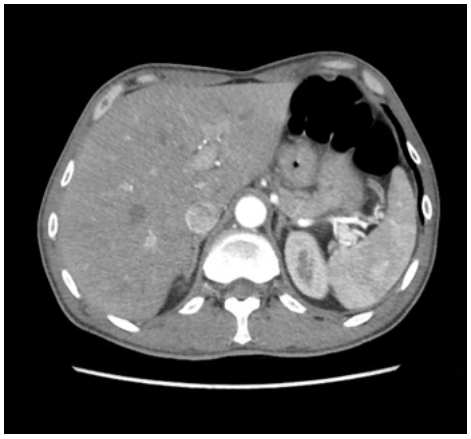

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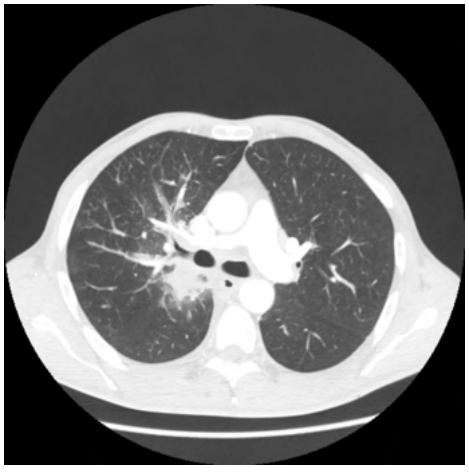

image 3

Conclusion: Ectopic ACTH producing tumor could be a difficult diagnosis when present with neurological symptoms. It should be considered especially in young adults with electrolyte disturbances. ll available techniques should be used to attempt a tumor localization and early treatment of these patients.
Disclosure: Nothing to disclose.

EPO-582

Hyperglycemia-related central pontine myelinolysis as a first manifestation of type 1 diabetes

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Background and aims: Central pontin myelinolysis is an osmotic demyelination syndrome, which occurs particularly due to increased osmolarity after rapid correction of hyponatremia. This syndrome was rarely described in other metabolic dysfunctions. We report an isolated case of pontin myelinolysis in a patient with severe hyperglycemia, in absence of hyponatremia.
Methods: Case report.
Results: A 25-year-old female known with celiac disease was admitted to our department for asthenia, acute confusional state and metabolic dysfunction with severe hyperglycemia and metabolic acidosis. Neurological exam at admission revealed confusional state and excessive daytime sleepiness. Some hours later, the patient presented axial and segmental ataxia with hypometria, horizontal nystagmus, dysarthria and mild paraparesis. The cerebral CT-scan described diffuse cerebral edema. Laboratory exams revealed fluctuating hyperglycemia, increased levels of glycosylated hemoglobin, significant glycosuria and ketonuria, inflammatory syndrome and normal natremia. Brain MRI scan revealed hyperintense pontine lesions in T2, T2FLAIR, restrictive in diffusion on DWI, and no focal contrast enhancements. During hospitalization the patient received corticotherapy, insulin, and after rebalancing the hydroelectrolytic and acido-base status, the evolution was slightly favorable with the improvement of the neurological symptoms and correction of the metabolic disturbances. On discharge the patient received oral corticotherapy and insulin with favorable outcome, symptoms resolving in less than six weeks.
Conclusion: Central pontin myelinolysis can be caused by hyperglycemia, especially in those cases with high fluctuations of glycemic values. In rare cases, central pontine myelinolysis can be the first manifestation of diabetes – in our case type 1 diabetes.
Disclosure: Nothing to disclose.

EPO-583

Atypical Wernicke encephalopathy presented as ataxia and severe bilateral hearing loss: a case report.

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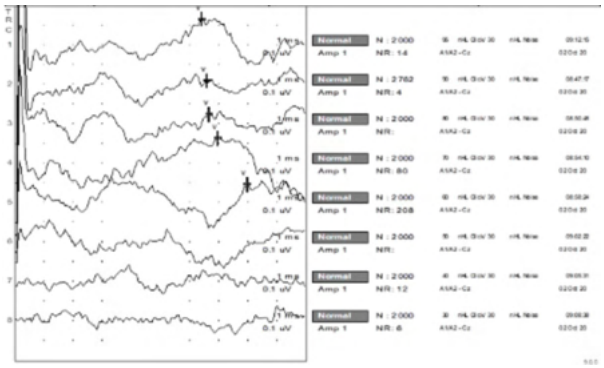
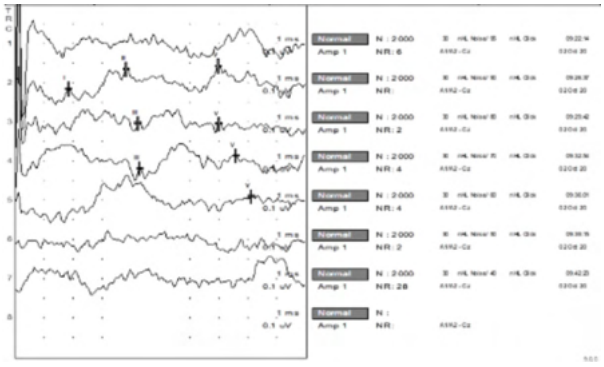
Background and aims: Report of an atypical case of Wernicke encephalopathy presented as subacute ataxia and severe bilateral hearing loss with great response to thiamine treatment.



Brainstem auditory evoked potentials for the left ear.



Brainstem auditory evoked potentials for the right ear.

Methods: A 62-year-old male presented subacute ataxia and severe bilateral hearing loss. Physical examination revealed cognitive impairment and inappropriate social behaviour (which were never reported before, as told by the patient's partner), and bilateral sixth cranial nerve palsy. No relevant findings were found after initial blood tests and microbiological and neuroimaging studies were performed. Brainstem evoked auditory potentials (BEAP) showed bilateral moderate-severe sensorineural hearing loss. Despite this finding, and considering the patient's history of chronic alcohol abuse (recently revealed in a precise anamnesis to the patient's partner), which suggested a possible Wernicke encephalopathy, thiamine levels were tested. Empirical thiamine treatment was initiated (500mg IV three times a day for two days and 250mg IV once a day for five additional days) until results of thiamine levels determination were given.
Results: Thiamine treatment resulted in total clinical hearing loss recovery within a few days, normalisation of bilateral sixth cranial nerve palsy, recovery of cognitive function and great improvement of walking ability; physiotherapy treatment commenced. Meanwhile, thiamine deficiency was confirmed, supporting the initial hypothesis of Wernicke encephalopathy. The patient was discharged from hospital continuing treatment with oral thiamine 100mg daily. Control BEAP were not performed since the patient died weeks later from unknown causes.
Conclusion: Hearing loss might be considered in the diagnosis of Wernicke encephalopathy as an infrequent symptom of this entity, with an excellent clinical response to thiamine treatment.
Disclosure: The authors declare no conflict of interest.

EPO-584

Genetic Susceptibility to Sarcoidosis: a study of a Tunisian cohort

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Background and aims: Sarcoidosis is multisystem disease results from interaction of environmental and genetic factors. The determinants of disease heterogeneity remain poorly understood. Our objective was to determine the predictive ability of genetic factors for disease risk and outcomes of patients with sarcoidosis.
Methods: A retrospective study including 65 patients diagnosed with sarcoidosis was conducted in the department of neurology and internal medicine of the Military Hospital of Tunis from 1997 to 2019. Genetic features were analyzed. DNA extraction was performed to determine frequencies of human leukocyte antigen (HLA) alleles and angiotensin converting enzyme (ACE) gene genotypes.
Results: We collected 65 patients with sarcoidosis. Genetic study concerned only 50 patients. A high frequency was found for the HLA DRB1 * 1,501 (38%) and HLA-DRB1 * 0301 (28 %). These alleles can confer a high risk of susceptibility to the disease. HLA DRB1 * 0301 is associated with a favorable course of the disease. The other alleles HLA- DRB1 * 1,106 and HLA-DRB1 * 0401 are found at lower frequencies (18% and 16% respectively). The frequency of genotype DD is higher than genotype II (30% vs 22%), similarly the D allele is present at 54% and I allele at 46%.
Conclusion: Because of genetic heterogeneity, further research is still needed to clarify the associations of the various genetic markers with risk and prognosis of disease, to personalized medicine approaches and improve outcomes of patients with sarcoidosis.
Disclosure: Nothing to disclose.

EPO-585

Takotsubo cardiomyopathy and internuclear opthalmoplegia – the clues for another diagnosis

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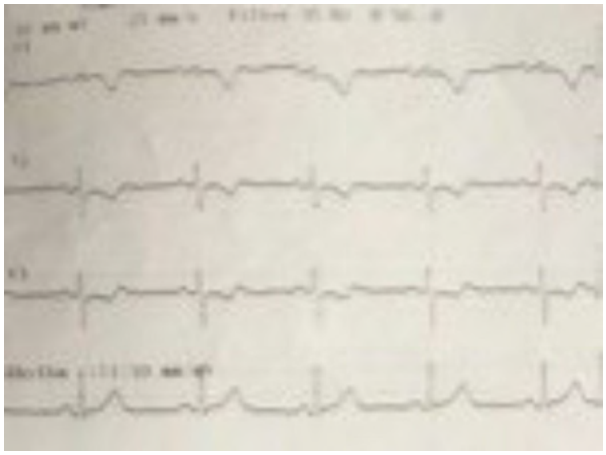
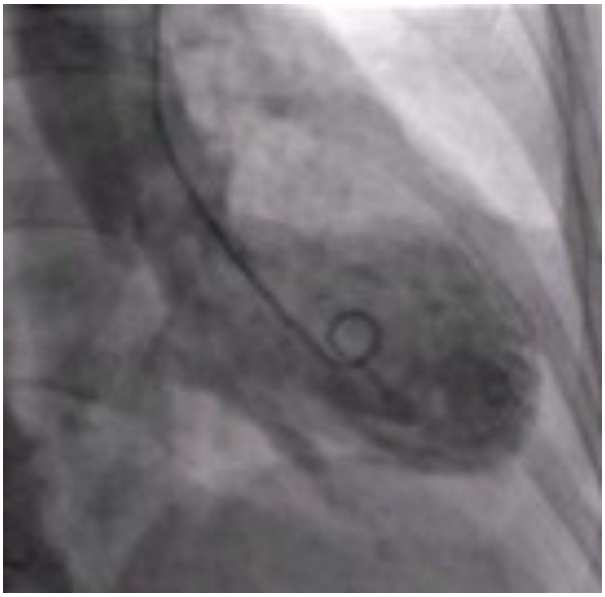
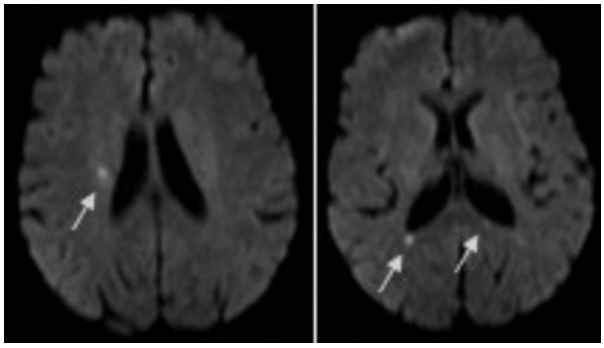
Background and aims: Sjogren's syndrome (SSj) is a systemic autoimmune disease characterized by lymphocytic infiltration of the exocrine glands (salivary and lacrimal) with neurological involvement in 20% of cases. CNS manifestations can result from diffuse (encephalopathy, cognitive deficits) or focal/multifocal impairment (motor/sensory deficits, seizures, movement disorders, cranial nerve palsies, myelitis). We present an unusual case of SSj with acute presentation of myocarditis and CNS vasculitis.
Methods: N/A
Results: A 65-year-old woman presented at the emergency department with acute chest pain, elevation of cardiac enzymes and V1–V3 T-wave inversions. Coronary angiography excluded obstructive coronary disease and revealed a characteristic Takotsubo cardiomyopathy pattern. Immediately after the procedure, she started complaining of binocular horizontal diplopia and bilateral internuclear opthalmoplegia was observed. MRI disclosed three small hyperintense lesions on DWI weighted imaging, in right internal capsula, periatrial and left splenium of the corpus callosum, reflecting acute lacunar lesions. Complete neurological recovery and cardiac improvement were achieved with corticotherapy. Complementary evaluation showed ESR elevation (54mm/h) and positive ANA (1/1,280), anti-SSA and anti-SSB antibodies. three-month history of generalized arthralgia and xerostomia/xerophtalmia were retrospectively identified. Salivary glands biopsy revealed sialoadenitis and confirmed Primary SSj diagnosis, allowing the integration of the acute clinical picture (sequential installation of myocarditis and cerebral ischemic lesions due to small vessel vasculitis).



Electrocardiography sowing V1-V3 T-wave inversions



Ventriculogram during systole demonstrating apical akinesis (takotsubo cardiomyopathy)



Brain MRI (1.5T) showing hyperintense lesions on DWI weighted imaging, in right internal capsula, periatrial and left splenium of the corpus callosum, reflecting acute lacunar lesions

Conclusion: SSj-related CNS manifestations usually precede the diagnosis, having small vessel vasculitis as the main underlying mechanism. A high index of suspicion is required in the presence of neurological manifestations and other systemic symptoms, in order to establish proper diagnosis/treatment.
Disclosure: Nothing to disclose.

EPO-586

Radicular pain as main complaint of Vitamin B12 deficiency

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Background and aims: Vitamin B12 deficiency is a multi-faceted disorder with symptoms ranging from neurological to psychiatric disabilities. We report a case with an uncommon complaint presenting as a painful radicular syndrome.
Methods: A 65 year-old patient with a two years history of gastric adenocarcinoma, who underwent total gastrectomy, was referred for proximal painful paresthesia and gait difficulties. He reported severe pain particularly on arising from a chair or while walking. Pain distribution included the posterior aspect of his thighs, sometimes reaching the soles, partially circumscribing bilateral S1 and S2 roots. His symptoms started two months prior to his neurological presentation. Neurological examination revealed slight paraparetic deficit, no tactile sensory deficit, minor proprioceptive deficit. His gait was slightly wide-based. The electrophysiological studies as well as his spinal and pelvic MRI were unremarkable. Metabolic screening revealed a low-normal serum vitamin B12 (293pg/ml), however with elevated values for methylmalonic acid (98 ug/l) and homocysteine (20.5umol/l). Additional biological assessment for infectious, autoimmune and paraneoplastic markers was negative.
Results: High-dose intramuscular cobalamin supplementation therapy was recommended. The patient had a complete recovery with absence of pain and no further complaints at follow-up, six months and 12 months later.
Conclusion: In patients at risk of cobalamin deficiency, even atypical presentations such as radicular symptoms should warrant metabolite testing despite normal vitamin B12 serum levels and be properly treated.
Disclosure: No conflicts of interest to disclose.

EPO-587

Hereditary Transthyretin Amyloidosis and Other Neuromuscular Diseases

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Background and aims: Hereditary transthyretin amyloidosis (hATTR or ATTRv [variant]) is a progressive, fatal disease caused by mutations in the transthyretin gene (TTR) and results in multisystem dysfunction. Early diagnosis, which can be facilitated with genetic testing, is key to achieving optimal patient outcomes.
Methods: This analysis utilised data from patients enrolled in hATTR Compass, a genetic testing programme for patients in the United States and Canada suspected of having or with a family history of hATTR with polyneuropathy. Next-generation sequencing was performed using an 81-gene panel associated with inherited neuromuscular disorders.
Results: A neurology specialist referred 188 patients who tested positive for a mutation and had a negative family history of hATTR. Of the 188 patients, 14 had a TTR mutation and 174 had non-TTR mutations. The most common TTR mutation was p.V142I (57%), which is typically associated with a cardiomyopathy phenotype. The most common non-TTR mutation was in the PMP22 gene (32%); this mutation is responsible for neuropathy arising from myelination errors in peripheral neurons. Compared to those with TTR mutations, the non-TTR mutation group had lower proportions of heart disease (9% vs 31%); bilateral carpal tunnel syndrome (22% vs 46%); and autonomic (28% vs 46%) dysfunction.
Conclusion: Diagnosis of hATTR is challenging because it can present similarly to other diseases. It is critical that clinicians recognise symptoms of hATTR and refer patients for genetic testing to facilitate diagnosis and initiate disease-modifying therapy for this fatal disease.
Disclosure: Funding was provided by Akcea Therapeutics, an Ionis Company; editorial assistance was provided by ApotheCom and scientific support was provided by Ambry Genetics.

EPO-588

Intracranial hypertension secondary to venous fistula in hemodialysis patient

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Background and aims: Intracranial hypertension is a serious complication that is usually associated with brain injury such as trauma, central nervous system (CNS) tumors, acute ischemic stroke, hydrocephalus, hepatic encephalopathy, or impaired CNS venous outflow. In addition, there is so-called benign intracranial hypertension, to distinguish it from secondary intracranial hypertension, which is typical in young overweight women.
Methods: We present an inusual case of secondary intracraneal hypertension in a 66 years old man with chronic renal failure in hemodialysis who came to hospital suffering from loss of vision in one eye since one week before.
Results: Bilateral papilledema was found in an ophthalmological examination and the lumbar punction demostrated an opening pressure of 35cm water with normal CFS contents, including autoimmunity, serologies and cultures. All the secondary causes where excluded wiht blood and neuroimaging tests. A flebography confirmed the present of a a stenosis and venous fistula of the right jugular and subclavian vein, where the patient was holding the hemodialysis catheter. Angioplasty was carry out, with improvement of papilledema in subsequent controls.
Conclusion: Managemet of intracranial hypertension depens on the etiology, so we consider it very important to make an early diagnosis. We have to consider the venous fistula as a possible cause of intracranial hypertension in patients who are carrying a catheter for haemodialysis in order to provide adequate treatment and thus prevent possible permanent vision loss.
Disclosure: Nothing to disclose.

Cerebrovascular diseases 5

EPO-589

Oculomotor manifestations in thalamic stroke. Systematic review of the literature

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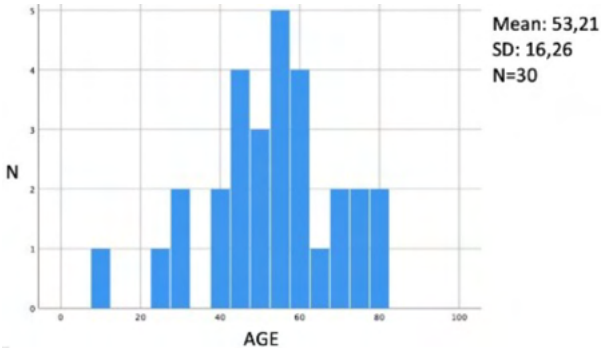
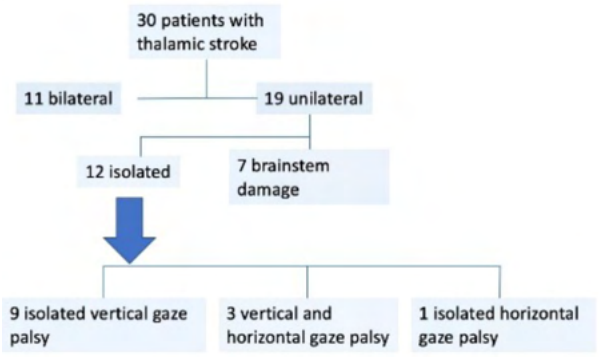
Background and aims: Ophtalmoparesis is a rare but known manifestation of paramedian thalamic infarcts, affecting mostly vertical gaze by interrupting corticofugal fibres to the interstitial nucleus of Cajal and rostral nucleus of the medial longitudinal fasciculus. We review the radiological and clinical characteristics of patients with ocular motility impairment after thalamic infarcts.
Methods: Systematic review (May 24 2020) in PubMed and EMBASE, keywords "(thalamus OR thalamic) AND(Diplopia OR ophthalmoplegia OR Gaze OR ocular) AND(stroke OR infarct OR infarction)" Inclusion: case reports
Results: We found 189 publications, 26 of them with a total of 30 patients with ocular motility affection after thalamic infarction, 55% were men, age 53 years (±16 SD). Only 38% referred to vascular risk factors. The most frequent etiology was unusual (13%), followed by atherosclerotic and cardioembolic (both 10%), not reported: 57%. In 11 patients, thalamic infarction was bilateral and in 19 it was unilateral; seven patiens with unilateral thalamic infartcs had also brainstem ischemia. From the isolated unilateral thalamic infarcts, in 75% (n=9) the ocular motility alteration affected exclusively the vertical plane, but 25% (n=3) presented with horizontal restriction, in one case in an isolated way. The affectation of ocular motility was bilateral in 25% (n=3). 91% of the bilateral infarcts were associated with ocular motility manifestations of both eyes, with vertical affectation in 100%, associating in addition alteration in bilateral horizontal motility in 36.4%.



Age distribution



Results

Conclusion: The thalamus plays a determinant role in the ocular motility, essentially vertical, but also horizontal, being this even the only manifestation of a thalamic infarction.
Disclosure: The author declares that he has no relevant or material financial interests that relate to the research described in this paper.

EPO-590

Cardiac papillary fibroelastoma: a threatening embolic source of stroke revealed by histopathology

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Background and aims: Etiological investigation in ischemic stroke constitutes a critical issue, for setting up tailored strategies of secondary prevention. Cardiac papillary fibroelastoma represents an under-recognized source of embolic stroke. We report two cases of ischemic stroke where histopathology aided in determining stroke etiology.
Methods: Specimens were processed for histopathology. Sections were stained with Hematoxylin and Eosin, Masson's Trichrome, anti-CD34(endothelial cells), anti-calretinin (mixomatous cells) antibodies.
Results: An 89-year-old woman was admitted after the acute onset of right hemiparesis and aphasia(NIHSS=18), due to occlusion of the left middle cerebral artery. Endovascular thrombectomy achieved complete recanalization(mTICI=3) after one pass of stent-retriever. Macroscopically the retrieved embolus appeared white, with multiple papillary fronds resembling a "sea anemone". The specimen was collected for histopathology. A 78-year-old man was admitted after the onset of dysarthria and right facial palsy(NIHSS=2). Brain MRI documented multiple cortical micro-ischemic lesions of both cerebral hemispheres. Transesophageal echocardiography documented a mobile excrescence arising from the left atrial wall. The cardiac mass was surgically excised and appeared highly friable. The specimen was collected for histopathology. Microscopic analysis of both specimens revealed a peculiar architecture with multiple projections, constituted of dense fibro-elastic matrix, surrounded by a single layer of endothelial cells, with high embolic potential. In both cases, histology confirmed a cardiac papillary fibroelastoma as embolic source.
Conclusion: Papillary fibroelastoma is a benign primary cardiac neoplasm that can easily embolize, leading to both large vessel and micro-embolic stroke. Surgical excision should be considered, to prevent recurrence.
Histopathology, including the analysis of retrieved cerebral thrombi, represents a significant adjunctive tool for stroke etiological investigation.
Disclosure: Nothing to disclose.

EPO-591

The impact of arterial hypertension to brain atrophy in patients with cerebral small vessel disease

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Background and aims: Cerebral small vessel disease (CSVD) is associated with arterial hypertension (AH), but the last one is also a risk factor of Alzheimer's disease. Thus, high blood pressure can be connected with the neurodegenerative processes in cerebrovascular diseases. The aim is the assessment of the impact of AH to brain atrophy in patients with CSVD.
Methods: The study included 65 patients (mean age 60.2±5.6, 42 women) with CSVD according to STRIVE criteria (2013) and the control group consisted of 12 volunteers (mean age 60.1±5.7 years, nine women). The brain
atrophy was studied with voxel-based morphometry using lateral ventricular volume, total gray matter (tGM), total cerebrospinal fluid (tCSF), total brain volume (TBV), total intracranial volume (TIV) and indices TBV/TIV and tCSF/TIV. All participants underwent 24-h ambulatory blood pressure monitoring (ABPM) for assessment mean and maximal values, standard deviation (SD) and the area under the curve (AUC) of daytime and nighttime systolic and diastolic blood pressure (SBP and DBP). The connections between parameters were studied with Pearson's correlation, where $p<0.05$ and $r>0.3$.
Results: Daytime SD of DBP was connected with tGM ($r=-0.314$), tCSF ($r=0.413$), TBV/TIV ($r=-0.426$) and tCSF/TIV ($r=0.426$). Mean daytime SBP was connected with tCSF ($r=0.311$) and lateral ventricular volume ($r=0.225$). Thus, the parameters of high blood pressure are associated with neuroimaging markers of brain atrophy.
Conclusion: AH plays role in neurodegenerative processes in the development of CSVD.
Disclosure: Nothing to disclose.

EPO-592

Differentiation of residual clot composition using dual-energy CT after endovascular stroke therapy: an in-situ study

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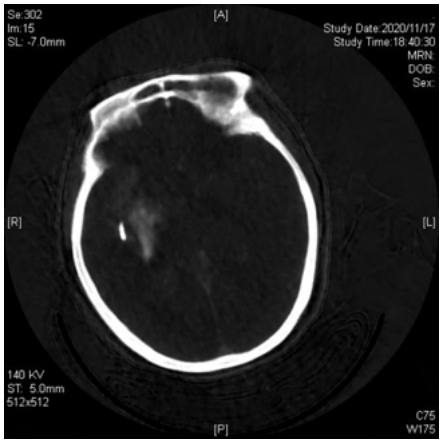
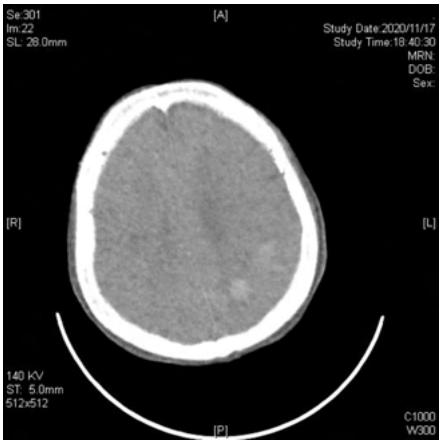
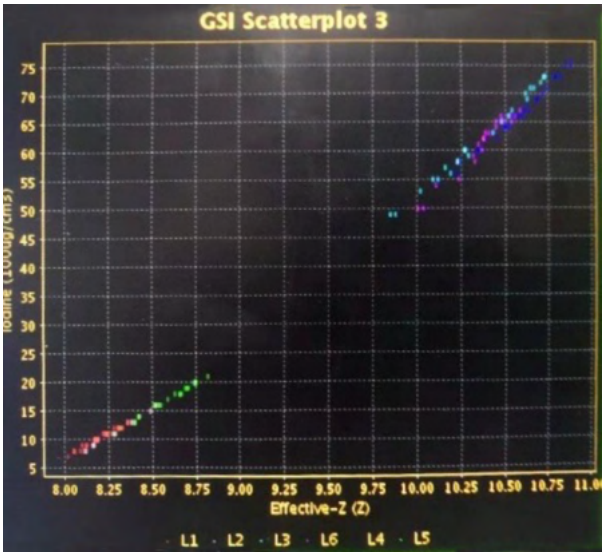
Background and aims: Dual-energy computed tomography (DE-CT) has been applied to differentiation between cerebral hemorrhage and contrast extravasation post thrombectomy in patients with acute ischemic stroke. There is growing evidence of using DE-CT to characterize clot composition in vitro. The aim of this study was to evaluate the capability of early post-procedural DE-CT, to distinguishing between fibrin- and red blood cell (RBC)-rich in-situ clots after thrombectomy.
Methods: We reviewed our prospectively collected imaging database for acute ischemic stroke patients with anterior circulation large-vessel occlusion, who received thrombectomy and underwent DE-CT (GE, 40~140keV) immediately and 16~24 hours after the procedures; and analyzed those who reached revascularization of mTICI 2b. Water-iodine and iodine-water density imaging were reconstructed to identify residual thrombi and hemorrhagic transformation. Virtual non-contrast (VNC) imaging and iodine overlap mapping (IOM) were processed to obtain quantified effective atomic number images of thrombi, compared with isolated contrast extravasation or intracranial hematoma in the database. Cardiac or arterial origins of embolisms were deductive according to preexist atrial fibrillation or carotid tandem lesions.
Results: Residual clots were detected by VNC imaging yielded at 70keV with highest contrast-to-noise ratio. RBC-rich clots from cardiac embolism had an average atomic number of 8.50 [8.00, 8.75] closer to hematoma (8.00 [7.75, 8.25]) or water (7.56), significantly differing with 10.5 [10.00, 11.00] of fibrin-rich clots closer to contrast extravasation, which attenuated after 24 hours.



Reconstructed iodine-water imaging showed a patient with a residual clot within M2 segment of right middle cerebral artery and basal ganglia contrast extravasation.



Reconstructed water-iodine imaging showed the same patient with isolated hematomas in the left occipital and parietal lobes.



Red blood cell-rich and fibrin-rich thrombi were quantitatively differentiated by average atomic numbers.

Conclusion: DE-CT may be valuable in the differentiation of fibrin- or RBC-rich residual clots after thrombectomy and consequently identify the embolic source of large-vessel occlusion in stroke patients.
Disclosure: Nothing to disclose.

EPO-593

Cerebral venous thrombosis due to overdrainage in a patient with normal pressure hydrocephalus

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Background and aims: Mechanical shunting of cerebrospinal fluid is an effective treatment for hydrocephalus but is not exempt from complications.
Methods: We report the case of a patient with cerebral venous thrombosis after ventriculoperitoneal shunting pressure adjustment.
Results: Clinical Case: A 67-year-old man with a history of normal pressure hydrocephalus and ventriculoperitoneal shunting one year ago, presented with gait disturbance and memory impairment. Head CT was normal, and the shunting pressure was reduced from 110 to 70mmH_20 with gait and memory improvement. One week later, he reported persistent pressure headache which worsen when lying down, accompanied with nausea and vomiting. His neurologic exam was notable for a short-stepped wide-based gait. During his stay at the emergency department, two generalized tonic-clonic seizures were observed. CT cerebral venography revealed middle and posterior third superior sagittal sinus, torcula, right transverse sinus and right sigmoid thrombosis and he was started on low molecular weight heparin and levetiracetam. EEG revealed bilateral frontal dysfunction without epileptiform activity. After two days, a new CT was performed and bilateral subdural hygromas were found. Shunting pressure was readjusted to 110mmH_20 and symptom improvement was noted.One week later, CT showed enlargement and bleeding of subdural collections. The drainage system was closed, and the patient continue to recover.
Conclusion: The temporal association between pressure adjustment and symptoms onset and the evidence of progressive subdural effusions suggest that the decrease of CSF volume by overdrainage leaded to an increase in cerebral blood volume and dilatation of venous sinus, which precipitated thrombus formation.
Disclosure: Nothing to disclose.

EPO-594

Association between hypertension and localities involved in hemorrhagic stroke

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Background and aims: Stroke is a significant cause of morbidity and mortality in Brazil, representing a serious public health problem. Among cerebrovascular diseases (CVD), hemorrhagic stroke is one of the most prevalent, with hypertension as the main cause. The study aims to analyze a association between hypertension and localities involved in hemorrhagic stroke, in a reference hospital in the Northeast.
Methods: It's a population based cross sectional study, performed by medical records of emergency patients seen in a reference hospital in 2019. Patients with a diagnosis of hemorrhagic stroke detected on brain CT were included, and patients with other intracranial comorbidities were excluded. The main predictor variables were: Age, Sex and hypertension. The outcome variable was location of hematoma. P values less than to 0.05 were considered significant.
Results: Temporal lobe was most affected by intraparenchymal (ICH) bleeding (28.2%), followed by the parietal lobe (26.8%), basal ganglia (26.8%), frontal lobe (25.4%) and thalamus (15.5%). There was a predominance of unilateral involvement (55%), with left hemisphere prevailing (57.5%) among hypertensive patients, while bilateral patients totaled 37.5%. Of patients, 7.5% had no bleeding in a specific hemisphere. More than half of patients with hypertension had subarachnoid bleeding (55%) and / or hemoventricle (60%).

Variables	Hypertensive Patients	Non-hypertensive patients	p(v)
Middle Ages)	63 anos	53 anos	0,015**
Age> 60 years (N (%))	22 (55%)	10 (42%)	0,009
Female gender (N (%))	23 (57,5%)	17 (55%)	0,823
Hemisphere E (N (%))	14 (35%)	7 (22,5%)	0,521
Subarachnoid (N (%))	22 (55%)	16 (52%)	0,799
Hemoventricle (N (%))	24 (60%)	12 (39%)	0,076
Thalamus (N (%))	6 (15%)	5 (16%)	0,885
Nucleocapsular (N (%))	14 (35%)	5 (16%)	0,076
Frontal lobe (N (%))	10 (25%)	8 (26%)	0,923
Parietal lobe (N (%))	8 (20%)	11 (35%)	0,136
Temporal lobe (N (%))	9 (22,5%)	11 (35%)	0,217
Occipital lobe (N (%))	3 (7,5%)	3 (10%)	0,736
Cerebellum (N (%))	3 (7,5%)	0 (0%)	0,12
Brainstem (N (%))	2 (5%)	1 (3%)	0,717

Table 1 * Chi Square Test; ** Spearman's ρ

Table 1 * Chi Square Test; ** Spearman's

Conclusion: In view of the divergent results of the current epidemiological propositions, this work concludes that there is a need for more investigations about the pathophysiology of hypertensive hemorrhages and as possible distinctions of this disease in a Northeastern population.
Disclosure: Nothing to disclose

EPO-595

Ischemic Stroke due to Spontaneous Reversible Extracranial Internal Carotid Artery Vasospasm: a Case Report

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[1] 3rd Department of Neurology, Istanbul, Turkey, [2] Acbadem University School of Medicine, Department of Neurology, Istanbul, Turkey

Background and aims: Reversible idiopathic extracranial internal carotid artery (ICA) vasospasm is a rare cause of ischemic stroke, in especially young patients, and is usually caused by mechanical manipulation, migraine headache, ergotism. The pathophysiology is not fully understood.
Methods: Case Report.
Results: A 23-year-old female patient presented with left hemiparesis and hemihypoesthesia. She had several similar reversible attacks which last about 30 minutes in the past years with no hospital admission. She had migraine-type headaches five times a month and bipolar disease history. MRI showed multiple infarction areas on the right middle cerebral artery (MCA) territory with no large vessel abnormality. We couldn't find any cardioembolic or other etiology except for a PAI-1 heterozygote 4G/5G mutation. She was discharged with warfarin treatment and had several ischemic attacks in different vascular areas in the following years with various treatment strategies. MR Angiography showed reversible stenosis of both internal carotid arteries (ICA) in every attack with different severities. All the attacks occurred while she was menstruating and after sleeping, suggesting hemiplegic migraine disorder. We diagnosed the patient with reversible vasoconstriction syndrome of the ICA and started prednisolone, nimodipine, and ASA treatment.
Conclusion: Spontaneous Reversible Extracranial Internal Carotid Artery Vasospasm is a rare condition with not well-understood pathology. Our case is a complicated example of this condition. Some cases have benefited from oral steroids and additional studies are needed to determine the optimal treatment.
Disclosure: Nothing to disclose.

EPO-596

Long-term safety and efficacy of carotid artery stenting – a prospective, single-centre study.

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[1] Department of Neurology Military Institute of Medicine, Warsaw, Poland, [2] Department of Neurology, Warszawa, Poland

Background and aims: There is a lack of long-term observations and data outside of controlled clinical trials in carotid artery stenting (CAS). The aim of this single center study was to evaluate the long-term effectiveness of CAS with embolic protection in a real-world setting
Methods: We prospectively followed-up consecutive 91 patients who had CAS performed between 2006–2016. Mean age was 65±9 years, 83% of subjects had symptomatic ICA stenosis, and 65% had at least three modifiable vascular risk factors. The median length of follow-up was 5.8 (interquartile range, 4.5–6.3) years.
Results: The rate of the primary end point (composite of stroke [rate of ipsilateral stroke was 13%], death, myocardial infarction, any revascularization procedure) was 35%. Relative risk (RR) was higher in subjects with mRS1 at baseline (RR 1.9, 1.2–2.4, p=0.01) or poor control of hypertension (RR 1.3, 95% CI 0.96–1.9, p=0.09). Patients with this end-point had significantly ($p<0.05$) higher MPV (10.7 vs 10.0 fL), systolic blood pressure (143.8 vs 131 mmHg) and creatinine level (1.12 vs 0.8mg/dL). The rate of in-stent restenosis (defined as 30% luminal narrowing at follow-up angiography) was 13%. The risk for in-stent restenosis tended to be higher in patients with ischemic heart disease (RR 1.9, 0.9–3.8, p=0.07).
Conclusion: In this study we confirm previously reported event rates and identify several risk factors for the composite outcome. Future studies are needed to confirm the importance of the identified risk factors and to assess their predictive ability.
Disclosure: Nothing to disclose.

EPO-597

Postprocedural Hemodynamic Instability after Carotid Artery Stent Placement

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Background and aims: The frequency, risk factors and long term consequences of postprocedural hypotension (PH) following carotid artery stenting (CAS) are not well known.
Methods: Prospective analysis of 30 patients with six-month follow-up undergoing CAS (self-expanding stent with an emboli-protection device). A validated 24-hour ABPM was taken 24 hours before and after CAS. PH was defined as systolic blood pressure (SBP)<90mmHg, or decrease in mean arterial BP (MAP) of 20% or systolic BP (SBP) of 30 mm Hg of baseline BP reading. Neurological assessment was performed 24 hours after CAS and at six month follow-up visit.
Results: Median age was 69 years, 70% were male, 86% of patients had symptomatic carotid stenosis. 20 patients (67%) experienced PH, 43% had transient bradycardia, 30% had both PH and bradycardia. The cumulated postprocedural mean SBP and DBP decreased from baseline 128/67mmHg to 108/54 mmHg ($p<0.01$), mean day (69/min) and night HR (58/min) decreased to respectively 58/min and 49/min ($p<0.01$). We found no association of HI with age, ischemic heart disease, bifurcation involvement, balloon size, inflation pressure, longer lesion length. Patients with PH significantly ($p<0.05$) less often were treated with Ca-antagonist (25% vs 70%), more often had ipsilateral ulcerated plaque (85% vs 50%) and had hemodynamically significant stenosis of contralateral ICA (60% vs 30%). During six month follow-up only one case of neurological deterioration was observed.
Conclusion: Postprocedural PH was a common phenomenon after CAS, however it was not linked with neurological complications. Patients at risk can be possibly identified through clinical and angiographic variables.
Disclosure: The authors received no specific funding for this work.

EPO-598

5 year follow-up of cryptogenic stroke patients following PFO closure

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Background and aims: According to guidelines PFO closure is recommended for secondary stroke prevention in patients with cryptogenic stroke. Paradoxial embolism from PFO mediated right to left shunt or cardioembolism has been described as the mechanism of stroke in these cases. The aim of the study was to follow-up stroke patients after PFO closure and determine the long-term effectiveness on reccurent stroke risk reduction.
Methods: 103 patients were enrolled in a prospective study and followed-up by phone up to five years after PFO closure. Standardized survey was conducted about their well-being, recurrent cerebrovascular events, and the use of prescribed medication. The pathogenic ischemic stroke subtypes were determined using CCS (Causative Classification System for Ischemic Stroke).
Results: 43,7% (n=45) of patients were male. The mean age – 44,4±13 (18-75). According to CSS 66,7% (n=58) of patients had possible cardio-aortic embolism (paradoxical embolism) and 19,5% (n=17) had evident small artery occlusion. Before PFO closure 91,9% (n=91) of patients had at least one cerebrovascular event (stoke or transient ischemic attack) and in five-year time after PFO closure recurrent cerebrovascular events were reported in only 5,1% (n=5) of patients, this difference is statistically relevant ($p<0.001$). 51% (n=50) of patients had complaints before PFO closure (headaches, fatigue, dizziness, visual impairment), and after PFO closure this number dropped to 38,8% (n=38), this difference is statistically relevant ($p=0.017$).
Conclusion: PFO closure might be effective in reducing recurrent cerebrovascular events. PFO is a possible risk factor for cryptogenic stroke in young adults. PFO closure can be associated with improvement of complaints.
Disclosure: This was an independent study, that did not require any funding.

EPO-599

The role of lipid imbalance and deregulated angiogenesis in the pathogenesis of Moyamoya angiopathy

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Background and aims: Moyamoya angiopathy (MA) is a rare cerebrovascular disorder characterized by ischemic/hemorrhagic strokes. The pathophysiology is unknown. A deregulation of vasculogenic/angiogenic pathways has been hypothesized as a possible pathophysiological mechanism. Since lipids are involved in modulating neo-vascularization/angiogenesis their deregulation is associated with cerebrovascular diseases. Our aim is to evaluate lipid and angiogenic/vasculogenic factor profile in plasma and Cerebral Spinal Fluid (CSF) of MA patients.
Methods: A subgroup of MA patients from GEN-O-MA project was included, with healthy donors (HD) and unrelated controls (UNR). Clinical data and plasma/CSF were collected. Angiogenic and inflammatory factor levels were measured by ELISA and a complete qTOF-MS-untargeted lipidomic analysis was performed on plasma/CSF.
Results: 39 MA adult, Caucasian patients, 32 HD and 48 UNR subjects were included. ELISA did not show differences for any of the tested factors in plasma of MA, HD and UNR. We observed a significant increase of VEGF-A and ANG-2 release in CSF from MA compared to UNR subjects. The lipidomic analysis showed an imbalance of specific lipid class levels in plasma and CSF of MA as compared to HD and UNR subjects.
Conclusion: Our findings suggest that both angiogenic and lipid pathways could play a central role in MA pathogenesis. The validation of results on a larger population and the correlation with clinical data could help our understanding of their role in MA, leading to the discovery of reliable biomarkers and the identification of therapeutic targets.
Disclosure: Nothing to disclose.

EPO-600

Cerebral venous thrombosis in spontaneous intracranial hypotension: a report of eight cases and review of the literature

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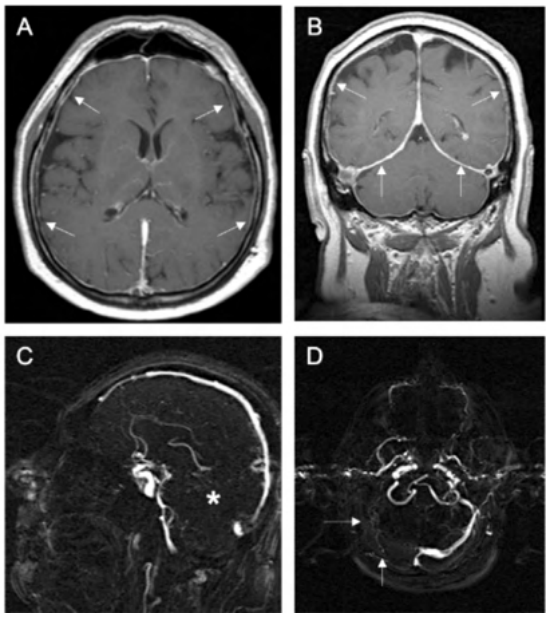
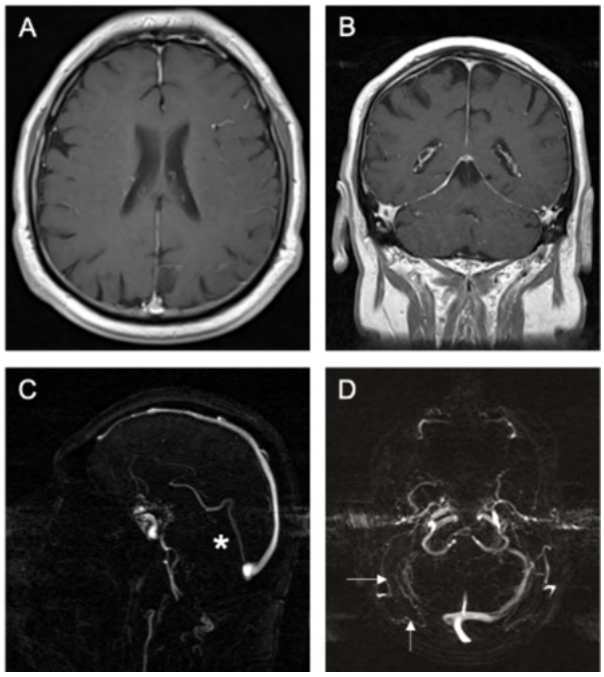
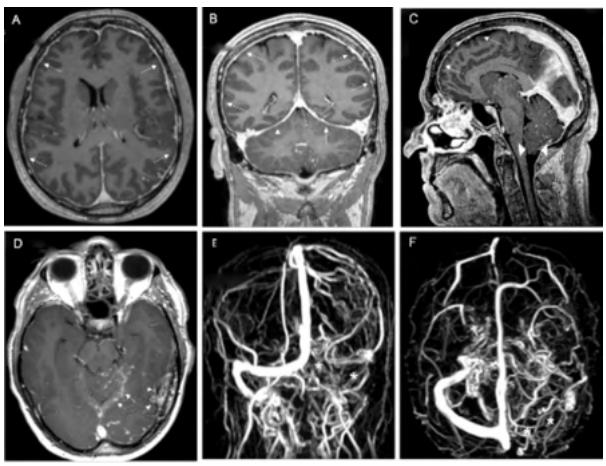
Background and aims: The occurrence of cerebral venous thrombosis (CVT) in patients with spontaneous intracranial hypotension (SIH) raises difficult practical questions regarding the management of the two conditions. The first-line therapy for CVT is anticoagulation (AC); however, its potential benefit in SIH/CVT patients, especially if complicated by subdual haematoma, must be carefully evaluated taking account of the intracranial haemorrhage risk. Venous system recanalization and good prognosis in SIH/CVT patients treated with epidural blood patch (EBP), the main treatment option for SIH, have been already described.
Methods: We reviewed our cases of SIH complicated by CVT among a cohort of 445 SIH patients observed and treated during the last years. All published case series reporting patients with SIH and CVT were also ascertained and reviewed.
Results: Eight (2%) out of 445 patients suffering with SIH, were also diagnosed with CVT. All patients observed had orthostatic headache, six out of eight patients received both AC and EBP treatments. Two patients were treated using only AC or EBP. A bilateral subdural haematoma enlargement after one month of AC was observed in one case. Complete CVT recanalization after treatment was obtained in three patients, including two with multiple CVT at baseline; partial CVT recanalization was achieved in two patients. Three patients experienced no CVT recanalization.



Brain magnetic resonance imaging (MRI) and magnetic resonance venography (MRV) before epidural blood patch (EBP) treatment in patient #1.



Brain magnetic resonance imaging (MRI) and magnetic resonance venography (MRV) eight months after epidural blood patch (EBP) treatment and anticoagulant therapy in patient #1.



Brain magnetic resonance imaging (MRI) and magnetic resonance venography (MRV) before epidural blood patch (EBP) treatment in patient #2.

Conclusion: The use of AC therapy should be weighed against the intracranial haemorrage risk and should be monitored carefully if initiated. Effective and prompt EBP, even without AC therapy, might lead to a good prognosis in selected cases.
Disclosure: Nothing to disclose.

EPO-601

Assessment of An Aphasic 'French-Turkish' Bilingual Speaker

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Background and aims: The number of bilingual adults with aphasia as a result of strokes has increased as the rise of bilingualism worldwide in recent years, causing a new challenge for language and speech therapies.
Methods: Here, we report a 68-year-old man with aphasia following an ischemic stroke attack.
Results: A 68-year-old right-handed male patient was admitted to the emergency department with the complaint of left-sided weakness. Diffusion weighted magnetic resonance imaging studies revealed acute ischemic stroke in the right middle cerebral artery territory (Figure). After one month following his stroke, his left-sided hemiparesis was recovered. However, he had another complaint. The patient was a retired teacher of French grammatic, and he said that he no longer can talk in French while he can understand it very well. He was referred to a speech therapist and one year after his motor aphasia in French recovered partially.

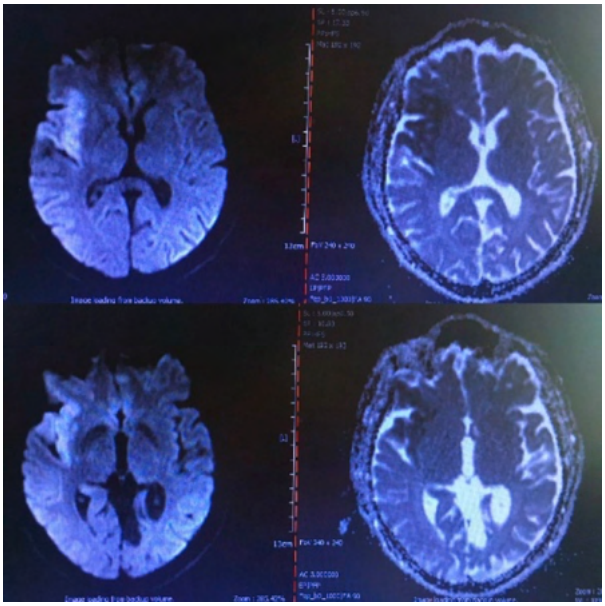

Figure: Diffusion weighted magnetic resonance imaging of the patient

Conclusion: In our case, although the patient was right handed; right hemispheric stroke caused an aphasia in his second language. This situation can be interpreted as the second language development can also have a control mechanism by the right hemisphere. This case study supports importance of comprehensive evaluation of both languages in an aphasic bilingual patient.
Disclosure: Authors have no financial disclosure.

EPO-602

Association between Cerebrovascular Disease and Restless Legs Syndrome

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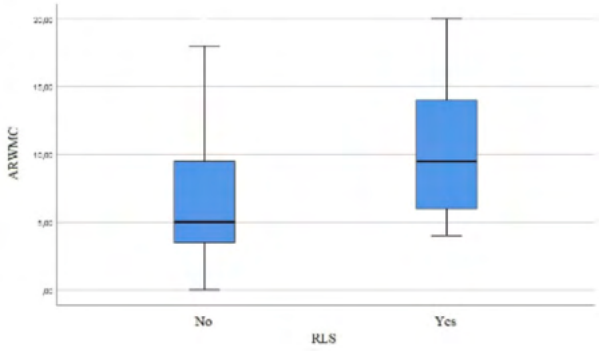
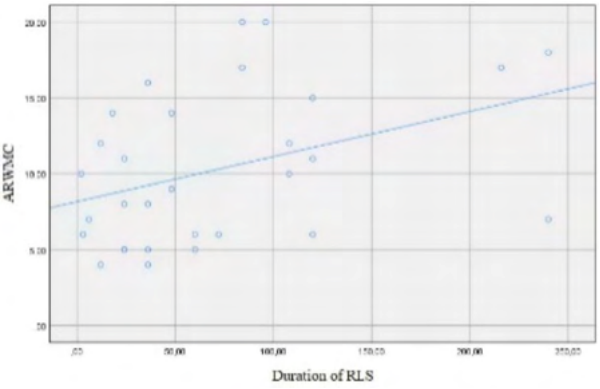
Background and aims: Cerebral Small Vessel Disease (CSVD) is characterized by lacunae, white matter hyperintensities, microhemorrhages, and perivascular spaces. Restless legs syndrome (RLS) is a sensorimotor disorder characterized by the desire to move the legs associated with unpleasant sensations. We aimed to determine whether RLS when combined with other cardiovascular risk factors causes an increase in CSVD burden in patients with transient ischemic attack (TIA) or minor ischemic stroke (MIS).

Methods: Between July 2018 and November 2019, patients who were hospitalized with TIA or MIS were interviewed, and RLS was questioned using the diagnostic criteria defined in 2014 by the International Restless Legs Syndrome Study Group. 109 patients were divided into two groups as those with RLS (n=30) and those without RLS (n=79). Demographics and stroke risk factors of patients; furthermore, RLS Severity Scale (IRLSRS) scores and duration of RLS (months) in the group with RLS were recorded. CSVD burden was measured in neuroimaging at diagnosis using the Age-Related White Matter Changes (ARWMC) Rating Scale and compared between the two groups.

Results: While there was no significant difference between the two groups in terms of demographics and stroke risk factors, ARWMC scores were found to be significantly higher in the group with RLS (p<0,001). While there was no correlation between IRLSRS scores and ARWMC scores, a significant correlation was found between the duration of RLS and ARWMC scores in the group with RLS (p=0,033).



Comparison of Total ARWMC Scores Between Groups



Correlation Between Duration of RLS and ARWMC Scores

Conclusion: The presence and duration of RLS may be an independent risk factor for CSVD in patients with TIA or MIS.

Disclosure: The authors report no conflict of interest.

EPO-603

Lemierre syndrome complicated with carotid artery occlusion

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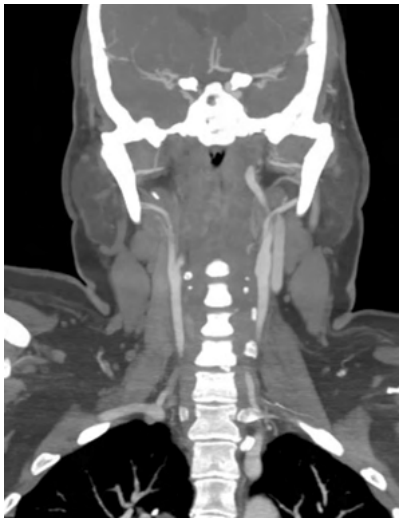
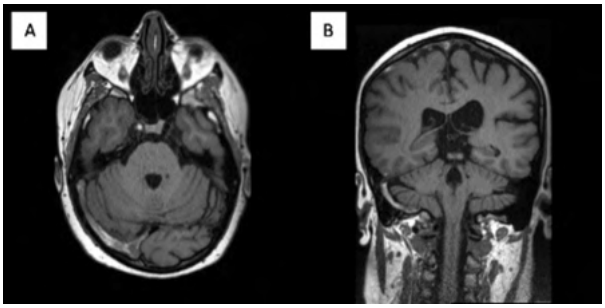
Background and aims: Lemierre syndrome consists of a thrombophlebitis of the internal jugular vein (IJV) in the setting of oropharyngeal infection. We present a rare case of Lemierre syndrome complicated with concomitant carotid artery occlusion.

Methods: N/A

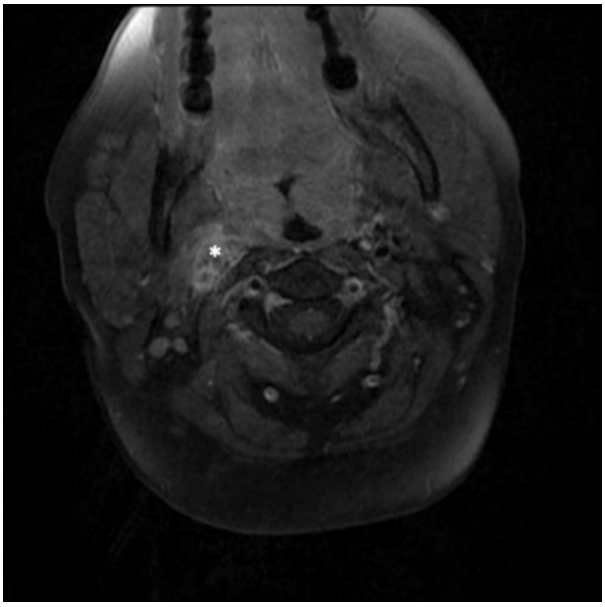
Results: A 35-year-old female patient, smoker, with morbid obesity and undergoing oral contraceptive therapy was admitted in the emergency department with a sudden onset of left superior limb weakness, paresthesia and ipsilateral involuntary movements. The week before, she had noticed odynophagia followed by headache and cervicalgia. Neurological examination revealed drowsiness and moderate left hemiparesis. Head and neck CT/CT-venography showed superior longitudinal, right transverse and sigmoid dural sinuses and ipsilateral IJV thrombosis, an expansive lesion on the right posterior parapharyngeal space and occlusion of right internal carotid artery (ICA). Patient started parenteral anticoagulation and on the first day of admission developed fever, increased inflammatory parameters and had two tonic-clonic seizures. MRI and MRV confirmed the CT findings and disclosed a right parapharyngeal phlegmon with compression of the right ICA, although an arthritic process could not be excluded. There were no signs of cerebral infarction. Antibiotherapy with meropenem was performed for 14 days. Blood cultures were negative. Patient improved significantly without neurological sequelae. Follow-up at three months with CT-angiography showed persistence of ICA occlusion.



CT-angiography, coronal image, showing occlusion of the right internal carotid artery and absence of flow on the ipsilateral venous jugular vein.



Axial (A) and coronal (B) T1-weighted MRI disclosing spontaneous hyperintensity at the right transverse and sigmoid sinuses.



Axial T1-weighted MRI with fat suppression and gadolinium showing inflammation at the right parapharyngeal space, with gadolinium enhancement (asterisk).

Conclusion: Lemierre syndrome is a potentially life-threatening disorder that is important to consider in patients with CVT, cervicalgia and high inflammatory parameters. Occlusion of the ICA has been rarely described. Local compression and arteritis are the two possible evoked mechanisms.

Disclosure: Nothing to disclose.

Clinical neurophysiology 2

EPO-604

Neurophysiological phenotypes of pharmacoresistant temporal lobe epilepsy

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Background and aims: If the results of clinical, neuroimaging and neurophysiological methods are discordant, then the localization of the epileptogenic zone is performed based on the results of long-term invasive monitoring of the bioelectrical activity of the cortex and deep structures of the brain. The aim of this work was to clarify the mechanisms of the formation of patterns of interictal and ictal activity in structural epilepsy.
Methods: The study included 35 patients (18 men, 17 women) with drug-resistant temporal lobe epilepsy, who were treated at the Polenov Neurosurgical Institute. The examination included video-EEG monitoring, long-term invasive monitoring of BEA of the cortex, and deep brain structures.
Results: The patients were divided into two groups according to the type of surgical treatment: 1) microsurgical resection of the epileptic focus, including the zone of structural changes (24 patients); 2) stereotactic destruction of the amygdala-hippocampal complex (six patients). The follow-up of the outcomes of the surgical treatment took place over 2–3 years. Depending on the results of the surgical treatment, the patients were divided into two groups: 1) patients with a favorable outcome (Engel 1–2) – 15 patients and 2) patients with no positive dynamics and a relatively poor outcome (Engel 3–4) – 15 patients. Five patients were excluded during the study.
Conclusion: The localization of the epileptogenic zone should be based on the cumulative assessment of interictal and ictal activity. The presence of more than one focus of interictal activity, the secondary spread of epileptiform activity from the primary focus, are prognostically unfavorable factors.
Disclosure: Nothing to disclose.

EPO-605

A retrospective review of repeated median nerve conduction studies in carpal tunnel syndrome

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[1] Clinical Neurophysiology Department in St Vincent's University Hospital, Elm Park, Dublin [4], Ireland

Background and aims: The natural history of carpal tunnel syndrome (CTS) is poorly understood. Patients with CTS are often referred for repeat NCS, mostly to follow up cases managed conservatively and where surgical outcome has been unsatisfactory. We aimed to describe the natural history of CTS in those who had conservative or surgical management.
Methods: We reviewed all NCS reports over a four-year period to identify patients with CTS who had repeated NCS. We collected information on demographics, initial and repeat NCS data, neurophysiological grade and types of intervention.
Results: We identified a total of 170 affected hands in 105 patients. The mean age of the initial NCS was 57±13 years (range 30–89). The mean interval between tests 5±4 years (range 0–21). Most cases were managed conservatively (n=112/170; 66%), and the remainder surgically (n=58/170; three 4%). Those that were managed surgically were more likely to have an improved outcome (χ^2=28.6; $p<0.001$); especially in those with severe CTS (χ^2=8.0; $p=0.018$), and unexpectedly in those with mild CTS (χ^2=16.6; $p<0.001$).
Conclusion: We made a surprising observation that those with mild CTS who were conservatively managed – the recommended treatment approach – tended to get worse or remain unchanged on repeat NCS; although there were small numbers in this group. Further prospective data on symptomatology and risk factors may help to identify a subgroup of mild CTS that would benefit from early surgical intervention.
Disclosure: Nothing to disclose.

EPO-606

High output current transcutaneous vagus nerve stimulation modulated cortical excitability in healthy participants

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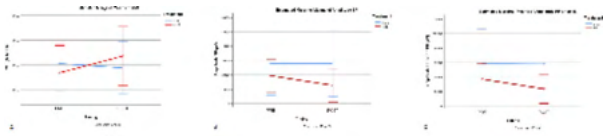
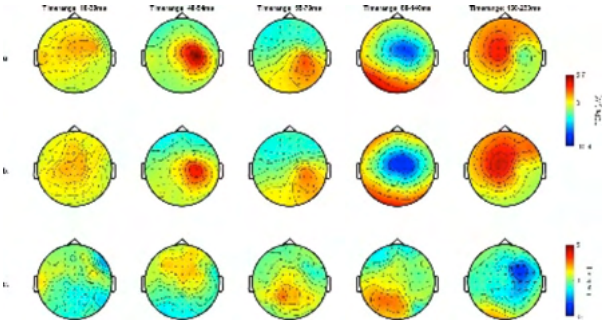
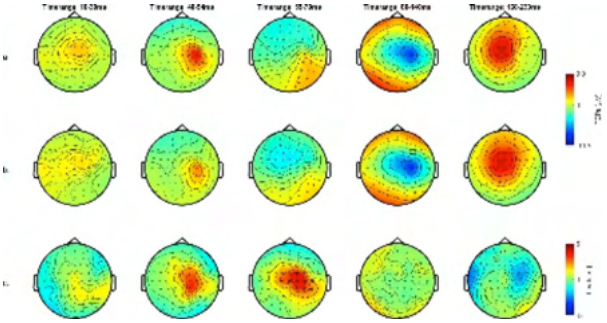
Background and aims: Transcutaneous Vagus Nerve Stimulation (tVNS) has been studied as a potential treatment for epilepsy with inconsistent results. Investigating the effect of tVNS on cortical excitability could provide insight in the mechanism of action and improve the stimulation paradigm. Cortical excitability can be measured with transcranial magnetic stimulation (TMS) combined with EMG and EEG, evaluating motor evoked potentials (MEPs) and TMS evoked potentials (TEPs).
Methods: In this prospective cross-over study, 15 healthy subjects were stimulated with tVNS and sham stimulation, delivered at the maximum tolerated output current. Single and paired pulse TMS was delivered at the right motor hotspot to evaluate MEP and TEP morphology before and after the intervention. MEP statistical analysis was conducted with a two-way repeated measures ANOVA. TEPs were analyzed with a cluster-based permutation analysis. Linear regression analysis was implemented to investigate an association with stimulation output current.
Results: tVNS did not modulate cortical excitability in this study. However an association was found between tVNS output current and MEP outcome measures indicating a decrease in cortical excitability as tVNS output current increased. A subanalyis of participants stimulated with tVNS output current above 2.5mA showed a significant increase of resting motor threshold, decrease of MEP amplitude and modulation of P70 and P180 TEP components.



Significant results of the MEP subanalysis in participants with stimulation output current >2.5mA by means of two-way repeated measures ANOVA.



Results of the single pulse TEP subanalysis in participants with stimulation output current >2.5mA. Topographical distribution of TEP amplitudes before (a) and after (b) active tVNS and T-statistic maps (c) of the TEP amplitude differences.



Results of the paired pulses TEP subanalysis in participants with stimulation output current >2.5mA. Topographical distribution of TEP amplitudes before (a) and after (b) active tVNS and T-statistic maps (c) of the TEP amplitude differences.

Conclusion: This study demonstrates the potential of tVNS to modulate specific markers of cortical excitability when high output currents are used. These findings stimulate the development of appropriate stimulation protocols for future studies investigating the effect of tVNS in epilepsy patients.
Disclosure: Nothing to disclose.

EPO-607

The using of functional myostimulation in combination with botulinotherapy for restore walking in patients after stroke

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K. Petrushanskaya, S. Kotov
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Background and aims: Training of poststroke patients to restore walking helps to increase the strength of paretic muscles, improve coordination of movements and stimulate functional recovery. However, spastic tone hinders rehabilitation.

Methods: We observed five post-stroke patients with walking disorders due to spastic hemiparesis (poststroke group, PSG). Botulinotherapy of spastic muscles of paretic leg was performed. Walking rehabilitation included functional myostimulation of leg muscles during walking training. Control group (CG) – five healthy individuals. To evaluate the results, «Biomechanics» complex (MBN, Russian Federation) was used.

Results: The walking function of PSG was significantly changed when compared with CG indicators: a 2.2 – fold decrease in movement speed to 0.52m/s, a 1.6 – fold decrease in the length of double step to 0.85m, and a 1.3-fold decrease in the pace to 73 steps/min. After botulinotherapy, there was a decrease in muscle spasticity by an average of 1.0 [0.0;1.0] points on the modified Ashfort scale. After course of rehabilitation using functional myostimulation, improvement in walking function was found according to biomechanics: the length of the double step, the speed and pace of walking increased, and the speed of the locomotor cycle decreased (Fig.). This led to the fact that the pace of walking and the time index of the step after rehabilitation did not differ statistically in PSG and SP.

Indicators	CG, n=10 M±m	PSG (n=5)		
		Day 0, M±m	Day 14, M±m	Dynamics (%)
Length of the double step, m	1,42±0,02	0,85±0,04^{A}	1,04±0,05^{B,C}	121
Duration of the locomotor cycle, sec.	1,21±0,03	1,57±0,06^{A}	1,29±0,04^{B,D}	82
Walking speed m / sec.	1,17±0,03	0,52±0,05^{A}	0,81±0,04^{B,C}	150
Walking pace, step/min.	99±1	73±2^{A}	88±2^{B,D}	119

Comment. CG - control group, PSG – poststroke group, A - p<0.05 between indicators CG and Day 0, B - p<0.05 between indicators Day 0 and Day 14, C - p<0.01 between indicators CG and Day 14, D - p>0.05 between indicators CG and Day 14.

Indicators of walking biomechanics in healthy individuals of the control group and group 1 patients before and after the rehabilitation course

Conclusion: The data obtained show a positive result of a combination of botulinotherapy and functional myostimulation to restore walking after a stroke.

Disclosure: There is not conflict of interest.

EPO-608

EEG characteristics in patients with autoimmune encephalitis

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Background and aims: EEG remains an important tool in the initial workup of autoimmune encephalitis (AE), although it is rarely specific. It provides information for the differential diagnosis, and it reveals subclinical seizures or non-convulsing status epilepticus.

Methods: We retrospectively reviewed the clinical, MRI and EEG data of patients diagnosed with definite antibody-mediated AE at the University Hospital of Tours between 2015 and 2019. Inclusion criteria were:
cell-surface or synaptic neuroglial antibody identified in either serum or CSF; at least one EEG at diagnosis and another either before diagnosis or during follow-up.

Results: 15 patients (mean age 61 [13–81]) fulfilled inclusion criteria. The following antibodies were identified: anti-LGI1 (n=6), anti-NMDAR (n=5), anti-GAD (n=2), anti CASPR2 (n=1), anti-GFAP (N=1). In total, 43 EEGs were analysed, nine done before diagnosis, 15 at diagnosis and 19 during follow-up. 11/43 (25.5%) were normal. Five patients with initially normal EEGs had abnormalities on later ones, mostly focal slowing. An abnormal posterior dominant rhythm was present in five patients, including three with anti-NMDAR, two presenting generalized rhythmic delta activity (GRDA). Focal theta or delta slowing was present on 44.1% EEGs, including on eight at diagnosis, when all involved temporal regions. five patients had abnormal EEG, but persistently normal MRI.

Conclusion: EEG can be normal at symptom onset in AE, but it becomes generally positive for interictal abnormalities if repeated during clinical evolution. Its diagnostic utility increases in the context of normal MRI. No specific pattern was found, except maybe for the association of GRDA with anti-NMDAR.

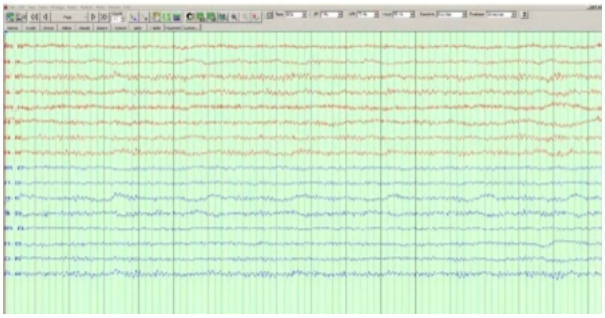
Disclosure: Nothing to disclose.

EPO-609

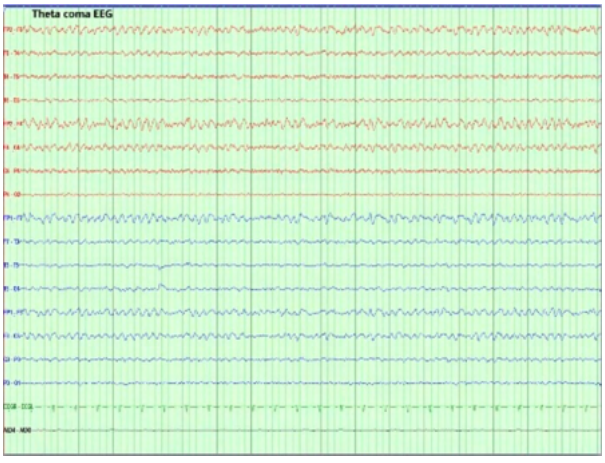
EEG findings in three cases of hanging

E. Tun [1], A. Al Samak [2], M. Thura [3], C. Mulligan [1], K. Lwin [1]
[1] *Clinical neurophysiology, Halifax, United Kingdom,* [2] *Leeds, United Kingdom,* [3] *Wolverhampton, United Kingdom*

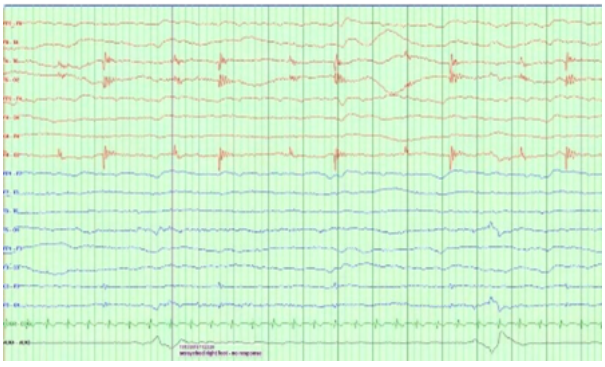
Background and aims: Hanging is the commonest mode of suicide in Asia and UK. In UK, suicide death rate is 10.9/100,000 population. Instantaneous death is due to direct injury to brainstem, cervical spinal cord and larynx. Delayed death from hanging is neurological and respiratory related complications. In one study of a tertiary care centre in UK, those died later (57%) had cardiorespiratory arrests as a common denominator.
Methods: Review of ICU-EEGs on three cases of hanging was made.
Results: Three male patients, age-26, 31 and 37 years old, were found hanging in the community. They all had mental health history and presented with cardiorespiratory arrests. CPRs were given and they were successful. All of them were intubated, ventilated and admitted to ICU. None had clinical seizures or myoclonic jerking. EEGs were obtained 36 to 72 hours arrests. Patients were comatose, unresponsive to any stimuli with intact brainstem signs. First patient's EEG is very attenuated background with slow delta. second patient's EEG is monomorphic rhythmical 5 Hz theta. Third patient's EEG has rhythmical 7–8 Hz pattern. They all were lacking in background reactivity and variability.



EEG alpha coma



EEG theta coma



EEG attenuated low voltage Delta

Conclusion: Outcome of suicidal hanging depend on the presence of cardiorespiratory arrest. All our patients had cardiac arrests and they all died 5–7 days after the event. Theta/alpha coma pattern and attenuated delta background, lack of reactivity and variability were seen on EEGs.
Disclosure: Nothing to disclose.

EPO-610

Abstract withdrawn

EPO-611

Early Observations of Using Percept™ INS for Sensing Local Field Potentials

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[1] Clinical, Minneapolis, United States, [2] Luven, Belgium, [3] Hoylandt, Belgium, [4] Merano, Italy

Background and aims: The new Percept™ primary cell implantable neurostimulator (INS) allows for simultaneous stimulation and sensing of local field potentials (LFP) in patients with deep brain stimulation (DBS) therapy. These LFP signals provide objective data that relate to the patient disease state and may be useful in patient management.

Methods: Sensing data was obtained from five subjects that were implanted with a Percept™ INS from Medtronic's Product Surveillance Registry (PSR). Built-in sensing features were used to assess patient-specific neurophysiological signals. BrainSense Streaming monitored for interictal spiking in epilepsy patients and allowed the clinician to record raw time-domain data while the patient was in the clinic. BrainSense Survey assessed for LFP activity in Parkinson's Disease (PD) patients. This feature obtains LFP signals from each bipolar pair and displays the results using a power spectral density plot. This allows the clinician to observe patient-specific peaks in the frequency domain.

Results: Interictal spiking was observed in epilepsy patients (Figure 1A). LFP peaks were identified within the beta band of PD patients (Figure 1B). The Percept™ system can track interictal spiking activity or LFP beta-band activity and can be used to provide insight into therapy effectiveness and potentially assist in programming optimization.

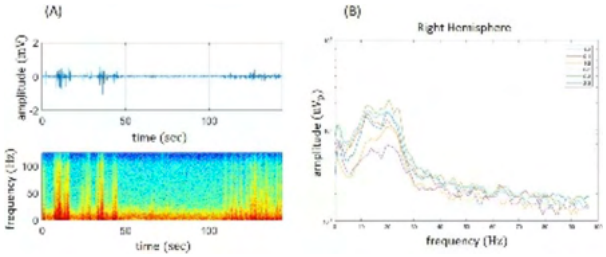

Figure 1. (A) Interictal spiking of an epilepsy patient recorded with Brain Sense streaming and (B) spatial overview of LFP signals in a PD patient recorded with BrainSense survey.

Conclusion: Sensing data from real world settings such as PSR, can provide invaluable objective data to help treat neurological symptoms related to diseases such as epilepsy and PD. This sensing capability is important for next-generation INS systems that will allow for automated sensing and stimulation, providing a step toward patient-tailored adaptive therapy.

Disclosure: Michelle Case, Alexa Singer, Kulwant Bhatia are employed by Medtronic.

COVID-19 5

EPO-612

The management of acute cerebrovascular disease at the time of Covid-19: retrospective study in Legnago stroke network

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Background and aims: During the Coronavirus-19 pandemic, global access to the emergency room (ER) was reduced (-43%); In this work we retrospectively assessed whether this phenomenon also occurred for accesses to the ER in patients suffering from acute cerebrovascular diseases, also evaluating any critical issues in the management of this pathology during the lockdown period.
Methods: All accesses in the ER for acute neurological event were examined in the months of March–April and May 2020, comparing them with those of the same period of the previous year. We also considered the systemic thrombolysis procedures performed in ischemic stroke in these two years to assess any temporal differences and the critical issues of management during the covid emergency.
Results: During the 2020 lockdown for the new Coronavirus, there were 44 visits to the ER for stroke (23 ischemias and 21 hemorrhages); in the previous year, in the same time interval, the accesses were found to have been 48 (28 ischemias and 20 haemorrhages) The systemic thrombolysis performed in 2020 were the same.
Conclusion: There were no statistically significant differences between 2019 and 2020 in the number of accesses in the ER for acute cerebrovascular disease Furthermore, the immediate definition of a therapeutic-diagnostic-course (with the immediate setting up of a "dedicated" Stroke Unit) for acute stroke-Covid 19 allowed the execution of thrombolytic treatment in all patients who are candidates for this procedure even before knowing the outcome of the covid-test (temporal criticality), thus guaranteeing the same time-dependent access modalities even during the covid emergency.
Disclosure: Nothing to disclose.

EPO-613

Neurological complications of Herpes Zoster, during convalescence from COVID-19 infection: Two clinical cases

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Background and aims: We are currently facing a new pandemic coronavirus. COVID-19 was shown to be linked with a continuous reduction in lymphocytes along the disease. Human alphaherpesvirus-3 (HHV-3) is a virus with the ability to establish latency in ganglionic neurons throughout the entire neuroaxis. After reactivation, HHV-3 causes herpes zoster, accompanied by skin shingles in a lot of cases. HHV-3 also infect the central nervous system (CNS). There are some scientific reports that HHV-3 complicate the course of COVID-19 infection; others that HHV-3 can be a marker for COVID-19 infection.
Methods: We report two cases of the infection of Herpes Zoster, during convalescence from COVID-19, followed by neurological complications.
Results: A 66 year old man during convalescence from COVID-19 presenting right facial herpes zoster (HZ) embracing I and II trigeminal divisions, after two months he develops postherpetic neuralgia. Another one, a 60 year old woman during convalescence from COVID-19 presenting with HZ in a left-sided Th7-Th8 dermatomal distribution and viral meningoencephalitis. It's important to limit contact of patients with HZ to avoid HHV-3 transmision to patients during recovery from COVID-19 infection, especially in elders. Antiviral treatment should be longer than usual.
Conclusion: Our report highlights that patients during convalescence period from COVID-19 must be monitored. Older people are at high risk for Herpes Zoster reactivation. Early treatment may be crucial and should be established in suspected cases. Nowadays telemedicine is impowered. That how we can prevent neurological complications from HZ during convalescence from COVID-19 infection.
Disclosure: Nothing to disclose.

EPO-614

COVID-19 infection in patients with multiple sclerosis in Castilla La-Mancha (Spain): multicenter study

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Background and aims: The emergence of the new SARS-CoV-2 coronavirus and the devastating pandemic derived from COVID-19 have hit Castilla La-Mancha (CLM) hard. Neurologists have had to make complex management decisions, particularly in patients treated with immunosuppressants, including those with multiple sclerosis (MS) on disease-modifying therapy (MST). However, it is unknown whether MS is associated with increased risk of infection or severity. Our objective is to describe the impact of COVID-19 on MS patients in CLM.
Methods: Observational, descriptive and retrospective, multicenter study in patients with MS and COVID-19 infection at the HG La Mancha Centro (Alcázar de San Juan) and CHU de Albacete between February and May 2020.
Results: 46 patients with MS and COVID-19 infection were recruited. The mean age was 42.2 years, the RRMS was 37% and the mean EDSS was 2.4; 30 with confirmation of infection, by PCR (33.3%), serology (26%) or both (34.7%); 37 (80.4%) were being treated with TME at the time of infection, remaining in 56.8% of them. Regarding the clinical manifestations, 38 (82.6%) had fever, 33 (71.7%) had respiratory symptoms and 31 (67.4%) had neurological; six (13%) patients had concomitant outbreaks or pseudo-outbreaks, eight (17.4%) required hospital admission, and 1 patient died of the infection.
Conclusion: Our experience leads us to think that patients with MS present an incidence and evolution of COVID-19 infection similar to other series of MS patients and healthy population with the same characteristics. The type of MSD and its duration do not appear to worsen the course of the infection.
Disclosure: Nothing to disclose.

EPO-615

Guillain Barré syndrome associated with SARS-CoV-2 infection

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Background and aims: COVID-19 is the disease caused by the SARS-CoV-2 coronavirus. The involvement of the infection at the respiratory level is clearly established. However, its neurological manifestations are less well known.
Methods: A 43-year-old male patient consulted for symmetric and global weakness of the four limbs of progressive intensity with inability to ambulation, as well as alteration in the sensitivity of the four limbs at the distal level. 10 days earlier, she had had a self-limited episode of diarrhea, followed by symptoms of an upper respiratory infection.
Results: The neurological examination revealed weakness of the four limbs and universal areflexia. The chest X-ray shows changes suggestive of incipient pneumonia due to COVID-19. SARS-CoV-2 PCR positivity is obtained. The conduction EMG study shows an increase in distal motor latencies and a decrease in sensory conduction velocities, as well as an increase in the minimum latency of the F wave for the right L5 and S1 roots, suggestive of demyelinating polyradiculoneuritis and compatible with the clinical suspicion of GBS.
Conclusion: The possibility of infection by SARS-CoV-2 is considered as a cause of GBS, however, it is prudent to assess chance in its presentation. The association between COVID-19 and GBS is not established, however, several cases have recently been reported that suggest the participation of the virus in its etiopathogenesis. It is important and necessary to deepen the study of the neurological manifestations of SARS-CoV-2.
Disclosure: Nothing to disclose.

EPO-616

Abstract withdrawn

EPO-617

COVID-19 AND CEREBROVASCULAR DISEASE

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Background and aims: Data is accumulating that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) can cause nervous system symptoms. CVD cases are increasingly reported as the presentation or during COVID-19. In this study, we aimed to evaluate the clinical findings of patients with a suspected and definite diagnosis of COVID-19 whom we evaluated for CVD.

Methods: A total of 43 patients who had CVD with a suspected or definitive diagnosis of COVID-19 were included in our study. Clinical characteristics, vascular risk factors (VRF), imaging and laboratory findings, and prognosis were recorded. Patients with positive nasopharyngeal swab SARS-CoV-2 PCR test and patients with negative PCR test were compared.

Results: 65.1% (n=28) of the patients were initially suspected of COVID-19 but PCR (-). While 10.7% of these patients were hemorrhagic CVD, 89.3% were ischemic CVD. The COVID-19 diagnosis of 34.9% of the patients (n=15) was confirmed by PCR or immunoglobulin tests. All of them were diagnosed with ischemic CVD. In 53.3%, the diagnosis of COVID-19 and CVD was made simultaneously. In 46.7%, CVD complaints developed 4–21 days after the diagnosis of COVID-19. 11 patients were diagnosed with CVD possibly associated with SARS-CoV-2, while four patients were considered to be atypical demyelinating/inflammatory disease probably associated with SARS-CoV-2 based on imaging and CSF findings. In the COVID-19 (+) group, the levels of fibrinogen, ALT, and the ratio of neutrophils/lymphocytes were significantly higher than the other group.

Conclusion: Increasing data provide evidence that acute CVD is not uncommon in COVID-19 and that elderly COVID-19 patients with VRF are more prone to CVD.

Disclosure: There is nothing to disclose.

EPO-618

Large vessel strokes in the elderly due to COVID-19 associated with poor outcomes

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Background and aims: Recent studies and observations have shown various thrombotic and thromboembolic complications from COVID-19 infection. Multiple mechanisms of hypercoagulability have been proposed: direct endothelial injury and invasion, increased circulating pro-thrombotic factors (including factor VII, fibrinogen), multiple coagulation abnormalities referred to as COVID-19 associated coagulopathy (CAC), and others. Updated guidelines recommend high intensity DVT prophylaxis in patients with COVID-19. Previous reports have outlined multiple cases of large vessel strokes associated with COVID-19. In some cases, stroke was the presenting symptoms of COVID-19 infection. Younger patients with few or no stroke risk factors generally have better outcomes.

Methods: We observed three cases of large vessel occlusion (LVO) strokes in elderly patients with symptomatic COVID-19 pneumonia and respiratory failure. Stroke diagnosis was made by clinical examination and neuro-imaging including computed topography (CT) and CT angiography (Figure 1 and 2). Patient characteristics, including past medical history and stroke risk factors, are detailed in Table 1. These patients remained critically ill throughout their hospitalizations.

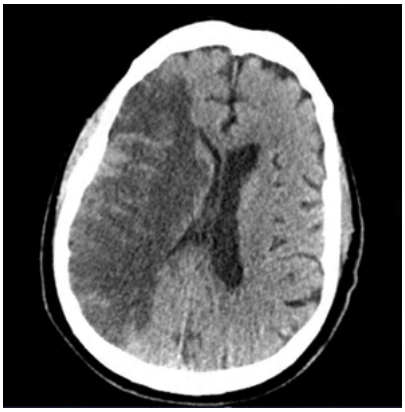

Figure 1: CT brain with large right MCA infarct with edema and mass effect.

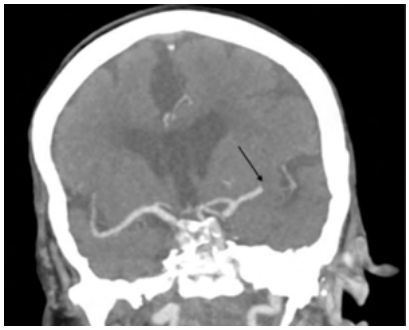

Figure 2: CT angiogram showing left MCA occlusion (arrow).

Table 1. **Clinical characteristics of 3 patients with Large-Vessel Occlusion Strokes**

Variable	Patient 1	Patient 2	Patient 3
Age (year)	89	77	79
Sex	Woman	Woman	Man
Medical history and stroke risk factors	Diastolic heart failure, COPD, hypertension, hyperlipidemia, dementia	Hypertension, hyperlipidemia, diabetes, rheumatoid arthritis, lung adenocarcinoma, stroke	Hypertension, hyperlipidemia, atrial fibrillation, Crohn's disease, obstructive sleep apnea
Medications	Amitriptyline, Metoprolol, Oxycodone, Lisinopril, Hydrochlorothiazide, Donepezil, Albuterol	Losartan, Hydrochlorothiazide, Insulin, Lexapro, Trazodone, Clopidogrel, Aspirin, Gabapentin	Citalopram, Hydrochlorothiazide, Metoprolol
NIHSS Score			
- On admission	14	14	26*
- At 24hr	14	23	26
- At last follow up	24	21	26
Outcome status	Hospice - died	Hospice - died	Hospice - died
Signs and symptoms of stroke	Global aphasia and right sided hemiparesis	Generalized tonic clonic activity followed by aphasia and right sided hemiparesis	Left sided hemiparesis, left facial droop and left gaze deviation
Vascular territory	Left Middle Cerebral Artery	Left Middle Cerebral Artery	Right Middle Cerebral Artery
Imaging for diagnosis	CT, CTA, MRI	CT, CTA, MRI	CT, CTA, CTP
Treatment for Stroke	t-PA	t-PA, MT	None/not candidate
COVID-19 symptoms prior to stroke	Syncopal episode, dyspnea	Fever, fatigue, dyspnea, seizure	Malaise, hypotension, cough, dyspnea

CT denotes computed tomography, CTA: CT angiography, CTP: CT perfusion, MRI: magnetic resonance imaging, t-PA: tissue plasminogen activator, and MT: mechanical thrombectomy
*Initial NIHSS upon transfer to our hospital

Table 1: Clinical characteristics of three patients with Large-Vessel Occlusion Strokes

Results: In this case series, all three patients died irrespective of aggressive therapies ranging from intravenous thrombolysis, mechanical thrombectomy (MT), and full dose anticoagulation.
Conclusion: COVID-19 associated hypercoagulability increases the risk of LVO strokes, and is associated with poor outcomes in older aged, high risk patients with underlying medical comorbidities and stroke risk factors.
Patients with severe infection may benefit from high intensity venous thromboembolism prophylaxis or even therapeutic dose anticoagulation, which may also lower risk of ischemic LVO strokes.
Disclosure: Nothing to disclose.

EPO-619

Increased number of stroke patients and thrombolysis during COVID-19 pandemic

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[1] Zarnesti, Brasov, Romania, [2] Brasov, Romania, [3] Department of Neurology, Brasov, Romania, [4] Ghimbav, Romania

Background and aims: The global pandemic caused by SARS-COV-2, has determined multiple changes in health care systems worldwide. These changes can also be seen in the decreased number of hospitalizations since this pandemic has started. This phenomenon can be caused by the measures taken by health authorities and by the fear of a COVID-19 infection, which discourage some patients to ask for specialized help in emergency departments.
Methods: This is a retrospective study in which we compare the number of hospitalizations, strokes and intravenous (IV) thrombolysis performed in our department, during March – December 2020, compared to March – December 2019.
Results: Compared to the same period of time of 2019, in 2020 the total number of hospitalizations has decreased with 17.18%. The most considerable decreases were reported in April (39.56%), October (34.37%) and November (35.07%). The number of patients hospitalized due to stroke increased (by 30.38%) between March December 2020, compared to the same period of 2019. Regarding the IV thrombolysis, it was noticed an increase in the number of thrombolysis by 33.54% performed in 2020, compared to the same period of 2019.
Conclusion: In our department, the decrease in the number of hospitalizations in April, October and November 2020 compared to the same months of 2019 may be due to the first and second waves of infections and the fear of a nosocomial COVID 19 infection. The number of patients with stroke has increased in 2020 compared to 2019, as well as the number of IV thrombolysis procedure.
Disclosure: Nothing to disclose.

EPO-620

Impact of COVID-19 on Care Delivered to MS Patients: Results From an International Survey of Healthcare Professionals

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Background and aims: The COVID-19 pandemic has presented challenges to health care professionals' (HCPs') ability to maintain standard of care for their patients with multiple sclerosis (MS). We present findings from a survey of HCPs about the impact of COVID-19 on their patients' well-being and care.
Methods: A 15-minute online questionnaire survey of HCPs treating patients with MS was conducted across Canada, France, Germany, Italy, Spain, the United Kingdom, and the United States between June 17 and July 22, 2020. The questionnaire covered the impact of COVID-19 on their patients' emotional health/well-being, changes and challenges in care, the role of telemedicine, and need for further support.
Results: Among 432 HCPs surveyed (general neurologists, 50%; MS specialists, 45%; MS nurses, 5%), 76% expressed concerns for their patients' overall health/well-being, with 61% worrying for patients' emotional status because of the pandemic. During the pandemic, 36% of HCPs were satisfied with their ability to provide care, versus 88% before the pandemic. Overall, 34% of HCPs were satisfied with remote/virtual Expanded Disability Status Scale assessments, with 61% expecting remote consultations to continue after the pandemic for test results, 54% for repeat prescriptions, and 46% for check-ups. HCPs also responded that information on how COVID-19 impacts MS (41%) and treatment (38%) would benefit patients, and about half suggested the pharmaceutical industry implement helplines (47%) and develop educational materials (49%).
Conclusion: Our survey revealed that HCPs have been worried about the standard of care during the COVID-19 pandemic and expect telemedicine to become an important part of MS care in the future.
Disclosure: Study support: Sanofi.

EPO-621

COVID-19 in multiple sclerosis and neuromyelitis optica spectrum disorder – The Czech experience

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Background and aims: 1 of the countries with the highest number of COVID-19 infected people per capita is the Czech Republic. The aim of this study is to evaluate the incidence, severity and outcome of SARS-CoV-2 infected multiple sclerosis (MS) and neuromyelitis optica spectrum disorder (NMOSD) patients.
Methods: From March 2020, Czech MS Centres were requested to report COVID-19 laboratory-confirmed MS/NMOSD patients. Data on demographics, MS type, history and severity, disease-modifying treatment (DMT), comorbidities and COVID-19 severity were obtained.
Results: We identified 428 (422 MS,six NMOSD; mean age 43.5; mean EDSS 2.8, median EDSS 2) laboratory-confirmed patients (PCR 92.5%; Antigen Rapid Test 0.9%, serology 7.5 %) with COVID-19 onset between March 16 and December 31. Mild COVID-19 course (no pneumonia) had 392 patients, more severe course 30 patients (5 deaths),six unknown course. Patients with more severe COVID-19 infection relative to patients with mild COVID-

19 course were older (mean 53.8 years vs 42.7 years), had higher EDSS (mean 4.3, median 4 vs mean 2.6, median 2) and had more frequent at least one comorbidity (50.3% vs 19.4 %). There was also a higher proportion of patients without DMT (40% vs 13.8%) and on anti-CD20 therapies (23.3% vs 8.2%) in more severe vs mild COVID-19 infection patients.
Conclusion: Majority of patients with MS had mild COVID-19 course. In the patients with more severe COVID-19 course, there was a higher proportion of patients without DMD, on anti-CD20 therapy, with higher degree of disability, with presence of comorbidities and in older age.
Disclosure: DS, DH, RA, MP, IS received support for research activities, speaker honoraria, consultant fees, compensation for conference travel or other activities with Biogen Idec, Novartis, Merck, Bayer, Sanofi Genzyme, Roche and Teva.

EPO-622

A rare case of Guillain-Barré syndrome presenting with COVID-19 infection in a six-year-old child

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Background and aims: Guillain Barré syndrome (GBS) is an acute inflammatory immune-mediated polyradiculoneuropathy characterized by rapidly progressing ascending weakness and hypo or areflexia. Severe acute respiratory syndrome coronavirus 2 (SARS COV-2) originating from Wuhan is spreading worldwide, and little information is available on its neurotropic characteristics. We report the first case of COVID-19 associated with GBS in a child from Santiago, Dominican Republic.
Methods: Case report.
Results: A six-year-old girl presented to our hospital with the complaints of cough, generalized weakness and unsteady gait. She had progressive weakness of distal lower extremities evolving to the upper limbs leading to quadriparesis. She also had walking and speaking difficulties. Her illness started with an upper respiratory tract infection one week back. Except for the prior respiratory illness, her past medical history was unremarkable. Physical examination revealed absent tendon reflex, weakness in the lower limbs greater than the arms. The sensory system was intact. Cranial nerves were also intact. Cerebrospinal fluid (CSF) revealed elevated proteins with typical albuminocytologic dissociation. CSF culture was negative. Four extremities electroneuromyography was performed and showed signs of acute polyradiculoneuropathy (Table 1). A PCR test for SARS-CoV-2 infection was positive. She was treated with intravenous immunoglobulins (IVIg) and recovered completely.
Conclusion: We conclude that although the incidence of COVD-19 in children is low, paediatricians must consider it while looking at patients presenting with acute flaccid paralysis and a recent history of respiratory tract illness. A thorough clinical and electrophysiological evaluation must be carried out for timely diagnosis and efficient management of these patients.
Disclosure: Nothing to disclose.

EPO-623

COVID-19 associated demyelinating disease: Case report and literature review.

R. Mathieu [1], L.A.R. Renteria [1], D.R. Soto González [1], R.I. González Gómez [2], G.E. Reyes Higuera [1], D.L. Lopez Rubio [1]
[1] Internal Medicine, Mexicali, Mexico, [2] Neurophysiology, Mexicali, Mexico

Background and aims: Introduction: The COVID-19 pandemic has put the medical world at a critical juncture, we are facing a disease that is heterogeneous and has presented clinicians with the reality of multiorgan involvement, that can develop even months after the initial infection. Most patients are asymptomatic, but some develop severe organ dysfunction, and while the most common is respiratory failure, the CNS is also involved. Regarding demyelinating diseases associated to COVID-19, there is limited data and case reports are few and far between.
Methods: Case report.
Results: Case presentation: A 33-year-old female patient with a history of systemic arterial hypertension and occasional alcoholism. She was admitted to the ER with weakness of the pelvic limbs and myalgias. Three weeks prior to admission, she developed asthenia, fever, adynamia, and dyspnea. PCR result for SARS-CoV2 positive. Upon admission, she presented weakness of the lower extremities, affecting her right body, was progressive, ascending, and made walking impossible, with hyperreflexia, dysesthesia, thoracic sensory level and loss of sphincter control, subsequently developing lagophthalmos, and dysarthria. CSF study, with mild mononuclear pleocytosis, oligoclonal bands were negative. MRI study showed demyelinating longitudinal myelitis, intramedullary lesions, hyperintense in T2, at the cervico-thoracic-lumbar levels. A PCR study for SARS-CoV2 in CSF was positive. Treatment was initiated with methylprednisolone boluses and IVIG.
Conclusion: To acknowledge the possibility of COVID-19 associated demyelinating disease in any patient with previous SARS-CoV2 infection and loss of consciousness, ataxia, epilepsy, encephalitis, myelitis or optic neuritis, associated with this emergent disease.
Disclosure: The authors declare that they have no conflict of interest to disclose

EPO-624

Role of medical interview during lockdown while pandemic in Croatia

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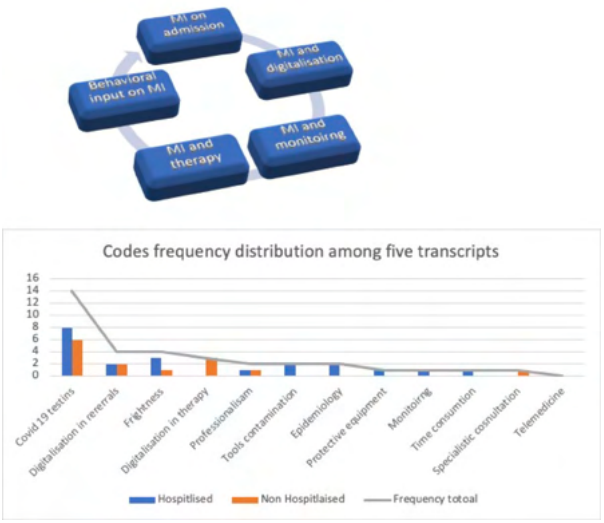
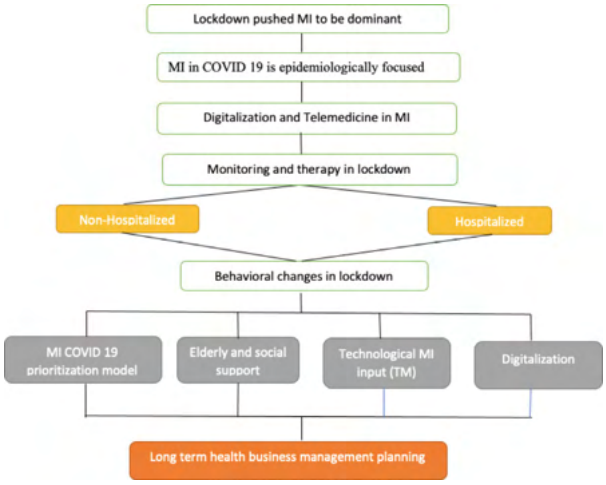
Medical, Rijeka, Croatia

Background and aims: This study is about questioning and evaluating the role of a medical interview (MI) among hospitalized and non-hospitalized individuals, positive on COVID 19, in lockdown circumstances. The role of digitalization and telemedicine (TM) in lockdown circumstances is evaluated in the context of MI, while the main research question is how and to what extent pandemic dictates modification of MI.
Methods: The research method applied is purposive sampling using qualitative code analysis of the interview's transcript of five representative participants. Five, interviewed participants with competencies to evaluate TM, digitalization and behavioral input in COVID-19 answered targeted questions. Pilot testing excluded patients in ICU (intensive care unit). Patients were divided into two groups, hospitalized and non-hospitalized group, and the goal was to investigate the importance of MI on both.
Results: Urgency, professional triage, and epidemiological approach were dictating MI structure in admittance. Inside of hospitalized group risk of contamination of tools was dominant what was the main obstacle to their wider applicability's. MI's role in monitoring and therapy in hospitalized patients was dominant in terms of epidemiological prevention during the patient's admittance. The importance of anxiety and fright is suppressive, inhibitory on MI.



MI functionality



MI long term input

Conclusion: MI in the observed population has a very low relation to telemedicine in hospitalized and non-hospitalized circumstances in Croatia. Findings can give input to COVID 19 hospitals to implement more telemedicine. Contrary to this digitalization in the Croatian health system is very much present in professionals.
Disclosure: Telemedicine and medical interviews haven't been demonstrating any connection in observed sample in Croatia that indicates a lot of room and potential for improvement.

EPO-625

Generalized myoclonus, associated with dysarthria in a COVID-19 patient

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Background and aims: Neurologic manifestations (myalgia, headache, anosmia and ageusia) or acute cerebrovascular diseases, skeletal muscle injury, encephalopathy, prominent agitation and confusion have also been reported in the spectrum of coronavirus disease 2019. Myoclonus is the term used to describe the sudden, involuntary jerking of a muscle or group of muscles caused by muscle contractions or muscle relaxation. In severe cases it can interfere with movement control and balance, eating or talking. Recently, a new cause of myoclonic jerks is COVID-19 infection. In these cases myoclonus may be multifactorial and represent a combination of hypoxia, medication toxicity and direct or para- infectious complications of the virus itself.
Methods: We report a case of a COVID-19 infection, a male patient by the age of 46.
Results: He was presented in our clinic on 3 December 2021 with generalized myoclonus associated with dysarthria. Myoclonus onset started on the 11th day of patient treatment for a bilateral interstitial pneumonia. No previous disease were reported and other causes of myoclonus were ruled out. Generalized myoclonus occurred spontaneously and were extremely sensitive to multisensory stimuli, predominantly involving the upper and lower muscles of the extremities and facial muscles resulting in movement disorders and dysarthria. Cerebral MRI was normal. We treated this patient with piracetam, rivotril and a reduction in myoclonic movements was observed five days after.
Conclusion: The occurrence of myoclonus during COVID-19 is a rare event that requires further investigation to clarify the full clinical spectrum of neurologic involvement and optimal treatment.
Disclosure: Nothing to disclose.

EPO-626

One year of COVID-19 pandemic in spinal muscular atrophy treatment and management – single centre experience

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Background and aims: Spinal muscular atrophy (SMA) is an autosomic recessive neuromuscular disorder, which affects mainly motor, but also pulmonary function of patients. In the last few years, natural history of the disease changed completely with novel treatments available. Nusinersen, an oligosense antinucleotide, was the first registered treatment for SMA and is widely used worldwide. Since the outbreak of COVID-19 pandemic, healthcare providers had to face enormous challenges. Neuromuscular centres needed to carefully measure benefits and risks related for the continuity of care for their patients.

Methods: In our centre we treat 63 SMA patients with intrathecal injections of nusinersen – 49 adults and 14 children. 27 patients receive injections under CT-scan, in the remaining 36 we administer the drug via standard lumbar puncture. We analysed treatment schedules during the pandemic and delays in dosing. We also report COVID-19 infection course in our patients. We highlight the main problems encountered by SMA-community during the pandemic.

Results: Besides the situation, treatment schedules were not significantly altered for nusinersen in our centre. COVID-19 infection in our SMA patients was mainly mild. Patients reported difficulties in access to physiotherapy and specialists consultations.

Conclusion: COVID-19 pandemic has greatly affected all medical institutions but long-term strategies are necessary to maintain the continuity of treatment and specialist care for SMA-patients.

Disclosure: Authors received lecture honoraria, institutional grant and consultancy fees from Biogen, Roche, PTC, Sanofi, Allergan and Novartis.

Motor neurone diseases 2

EPO-627

Phenotypic heterogeneity of C9orf72 gene expansion in a Portuguese family

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Background and aims: The expansion of GGGGCC hexanucleotide of C9orf72 gene is the most frequent mutation of familial and sporadic cases of amyotrophic lateral sclerosis (ALS) and/or frontotemporal dementia (FTD). It is present in 10% of total cases in Europe, in a dominant autosomal hereditary pattern. It is characterized by its broad phenotypes' spectrum, which includes primary lateral sclerosis, atypical parkinsonism, or Huntington-like disease, besides ALS and ALS-FTD.
Methods: Case report.
Results: We present two C9orf72 positive siblings with different clinical manifestations regarding disease presentation, age onset and progression. They had maternal history of probable of ALS. One of the siblings, a man, present at the age of 74 years with a spinal-phenotype of ALS, with upper (UMN) and lower (LMN) motor neurons clinical signs. The other, woman, currently with 65 years old, presented with akinetic-rigid parkinsonism at 55, followed by UMN signs of upper and lower limbs, without clinical or neurophysiological signals of LMN loss. DAT-scan® revealed functional involvement of nigro-striated. Genetic testing of both siblings revealed an expansion of 30 and 90 repetitions of C9orf72 hexanucleotide, respectively.
Conclusion: This family reflects the phenotypic heterogeneity associated to expansion of C9orf72 gene, which is still to elucidate, but can be explained by variations on the number of hexanucleotide repetitions, as well due to interactions between the gene and environmental and epigenetic factors.
Disclosure: Nothing to disclose.

EPO-628

Primary Lateral Sclerosis Post Poliomyelitis

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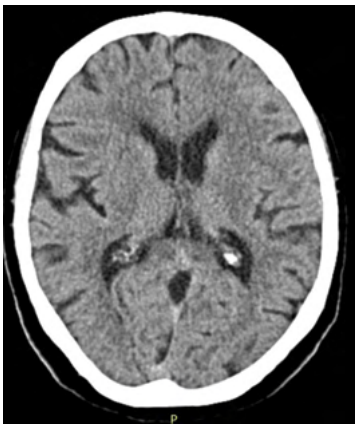
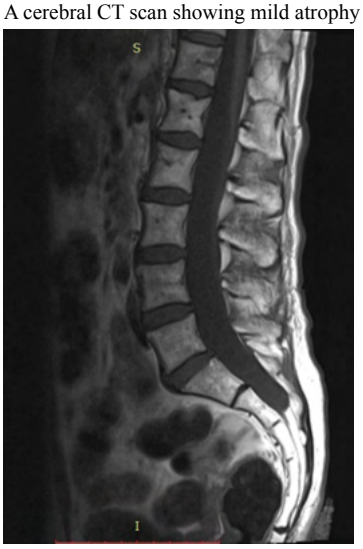
Background and aims: A 64-year old woman previously diagnosed with poliomyelitis on her right leg arrived in the emergency room with progressive left sided muscle weakness that had started approximately three years prior. The patient suffered from poliomyelitis at the age of seven months and since then had no complaints until she came into our ER.
Methods: An MRI of her spine showed important degeneration of the vertebrae and neurological exam, cerebral CT scan and EMG ruled out the suspicion of amyotrophic lateral sclerosis and post polio syndrome but didn't give any definitive diagnosis. A two-year follow up showed the patient had almost a complete loss of mobility and the Babinski sign present on her left side.



A cerebral CT scan showing mild atrophy



An MRI showing degeneration of the lumbar area

Results: A follow-up EMG now showed an important progression of an upper motor neuron disease ultimately giving a diagnosis of primary lateral sclerosis.
Conclusion: Primary lateral sclerosis isn't a well known complication of poliomyelitis. It was interesting that it came on the contralateral side of where she originally suffered polio, showing that the damage to the anterior horns of the spinal cord could have long-term effects.
Disclosure: Nothing to disclose.

EPO-629

Nusinersen treatment of adult patients with spinal muscular atrophy: Clinical experience from Slovenia

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Background and aims: Since the approval of nusinersen for treatment of spinal muscular atrophy (SMA) in Slovenia in March 2019, adult patients with SMA are receiving treatment at our neuromuscular centre at the University Medical Centre Ljubljana. Our aim is to present our experience with the nusinersen treatment and preliminary treatment results.
Methods: 38 adult patients are receiving intrathecal nusinersen at our centre using standard lumbar puncture or cone beam CT guided intrathecal application. Functional assessment is performed at recruitment, before treatment and everysix months during treatment using Hammersmith Functional Motor Scale Expanded (HFMSE), Six Minute Walk Test, Revised Upper Limb Module and spirometry.
Results: 19 patients are receiving nusinersen using standard lumbar puncture and 19 using cone beam CT. All the applications were technically successful. 81% of the cone beam CT applications were transforaminal, the rest interlaminal. Preliminary results based on HFMSE and spirometry show some functional improvement or stabilization of functional status during treatment in approximately two thirds of patients. Patients subjectively reported more energy and strength, more effective cough and better sleep. Most common side effects included headache and/or back pain following application and tiredness.
Conclusion: Nusinersen treatment seems to improve or stabilize functional status of most SMA patients. Nusinersen application was feasible in all adult SMA patients, including those with severe scoliosis. Cone beam CT guided intrathecal application is safe and successful.
Disclosure: Nothing to disclose.

EPO-630

Nusinersen treatment in adult patients with 5q spinal muscular atrophy

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Background and aims: To assess safety and efficacy of nusinersen in adult 5q spinal muscular atrophy (SMA) patients.
Methods: Longitudinal data of adult SMA patients were collected retrospectively and prospectively in five centers. Patients were followed at least for six months with one motor scale (Hammersmith Functional Motor Scale Expanded –HFMSE-, Revised Upper Limb module –RULM-). Clinical and patients' global impression of change (CGI-C and PGI-C) were recorded in treated patients at the last visit. Functional scales (Egen Klassification, EK2; Revised Amyotrophic Lateral Sclerosis Functional Rating Scale, ALSFRS-R) and forced vital capacity were collected when available.
Results: 79 SMA patients (39 treated with nusinersen) were included. Compared with untreated patients, treated patients showed an improvement of two points (0.46) in RULM ($p<0.001$) after six months; and an improvement of one (0.02) point in HFMSE ($p<0.001$), 1.5 (0.46) points in RULM ($p=0.016$), and -3.9 (1.6) points in EK2 ($p=0.018$), after a mean follow-up of 16 months. According to the CGI-C and PGI-C, 64.1% and 61.5% of treated patients improved. Being non-sitter was associated with less response to treatment, while longer time of treatment was associated with better response. Most patients (77%) presented at least one adverse event, mostly mild.
Conclusion: This multicenter study provides class III evidence that nusinersen is effective in at least a subset of SMA patients, and causes frequent mild adverse events. Response to nusinersen is variable, though overall mild, in adult SMA patients. Most severely affected patients with complex spines are probably those with the most unfavorable risk-benefit ratio.
Disclosure: I have served on advisory boards for Biogen and Roche and received travel and speaker honoraria from Biogen and Roche.

EPO-631

Respiratory function evaluation in treatment – naïve patients with Spinal Muscular Atrophy

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Background and aims: Spinal muscular atrophy (SMA) is categorized into five main types (0, I, II, III, IV) based on the age of onset and the highest level of motor function achieved. Notwithstanding that respiratory failure is the main cause of mortality, especially in SMA type I and type II, little is known about the respiratory function in SMA. The new therapeutic era has merged the necessity to explore new outcome measures in order to evaluate the effects of treatment.

Methods: We analysed Forced Vital capacity (FVC), forced expiratory volume in one second (FEV1), peak expiratory flow (PEF), maximal inspiratory (Pi max) and expiratory (PE max) pressures in 20 individuals (17–67 years) with genetically confirmed SMA type II(n=10), type III(n=8), type IV (n=2).

Results: A progressive decline was observed in the respiratory parameters in SMA type II whereas respiratory function was less affected in SMA type III and IV. There was a statistically significant difference between different SMA types in FVC, FEV1 and PEF Predicted ($p<0,05$). As expected, the baseline values of FEV1, FVC and PEF were significantly lower in SMA type II patients. (Range %FEV1:16%-81%, %FVC:20%-84%, %PEF: 17%- 81%). Typically, the expiratory muscles were more affected than the inspiratory muscles in all SMA types.

Conclusion: The progressive decline in respiratory muscle strength is expected in SMA type II and IIIa. The evaluation of respiratory muscles is not only necessary for an early intervention in order to improve survival in SMA patients but also it could be considered as an outcome measure for treatment's effectiveness.

Disclosure: Nothing to disclose.

EPO-632

Anxiety and depression in patients with ALS.

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Background and aims: The literature describes that the affective disorders in ALS may be overestimated, because questions about the physical symptoms of the disease in the depression rating scales, which may not be associated with the depression.

Methods: We examined 180 ALS patients on the HADS scales. The patients were re-examined six months later, then a statistical analysis was carried out.

Results: The level of anxiety and depression according to the HADS scale was determined in 44.4% (80 patients). The mid-point of anxiety was 6.0 points (Q1=3,0, Q3=8,0), and the level of depression was 6.0 points (Q1=3,0, Q3=9,0). In the structure of affective disorders, sub-anxiety disorders predominated in 31.25% (25 patients). Subclinical depression occurred in 22.5% (18 patients). Valid cased depression was detected in 15% (12 patients), while anxiety disorders were detected in 8.75% (7 patients). Our patients were offered pharmacotherapy to reduce affective disorders. 22.2% (40 examples) took antidepressants. 8.8% (16 patients) refused to take antidepressants, 25% (20 patients) tried to hide the illness from some relatives and friends. Testing on this scale in dynamics after six months was carried out in 28.3% (51 patients). The level of anxiety in the dynamics decreased to 4.0 points (Q1=3.0, Q3=6.0), the level of depression - to 5.0 points (=3.5, Q3=7.0), which is statistically significant.

Conclusion: Most of the patients have doubtful cases of behavior and depression. Antidepressants and neurologic monitoring helped reduce anxiety and depression on the HADS scale.

Disclosure: Nothing to disclose.

EPO-633

Gene replacement therapy for symptomatic spinal muscular atrophy type 1: final results of the Phase III STR1VE-EU study

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Background and aims: STR1VE-EU (NCT03461289) was a European, multicentre, single-dose, open-label Phase III study of onasemnogene abeparvovec for patients with spinal muscular atrophy type 1 (SMA1).

Previously presented interim results from STR1VE-EU demonstrated the efficacy of onasemnogene abeparvovec through December 2019. Here we report final results of the study.

Methods: SMA1 patients <6 months of age received a one-time IV infusion of onasemnogene abeparvovec (1.1 X 10E14 vg/kg). Efficacy outcomes were independent sitting 10 seconds (WHO criteria) up to and including the 18 months of age trial visit (primary efficacy endpoint), survival (no death or permanent ventilation) at 14 months of age, both compared with PNCR natural history data. Safety outcomes included adverse events (AEs) and laboratory results.

Results: Last patient last visit was September 11, 2020. 32/33 patients completed the study. At baseline, mean age was 4.1 months and mean weight was 5.8 kg (Table 1). 14/32 patients (44%) achieved the primary endpoint, and 31/32 (97%) survived without permanent ventilation (both p<0.001 vs. PNCR; Table 2). 32/33 (97%) patients experienced 1 AE, and six patients (18%) exhibited 13 serious treatment-related AEs. Review of objective data including vital signs and laboratory findings did not reveal new/emerging safety signals. One death unrelated to treatment was reported.

Table 1. Demographics and Baseline Clinical Characteristics in STR1VE-EU

Characteristic	STR1VE-EU (N=33[a])	STR1VE-US (N=22[b])
Mean BMI in kg/m^2 (range)[c]	15.1 (12.1 - 20.4)	15.4 (13.0 - 20.0)
Patients who could swallow thin liquids (%)	31 (93.9)	22 (100)
Patients requiring feeding support (%)	9 (27.3)	0 (0)
Patients requiring ventilatory support (%)	9 (27.3)	0 (0)
Patients hospitalized prior to dosing (%)	22 (66.7)	17 (77.3)

kg=kilograms, m=meters, BMI=body mass index.
[a]33 patients treated, one patient dosed at 181 days and so not included in the intention-to-treat (ITT) population (N=32).
[b]22 patients treated, all in the ITT population (N=22).
[c]Weight (in kg)=weight (in lbs)*0.4536, length (in cm)=length (in inches)*2.54, BMI (kg/m^2)=Weight (kg)/[Length(m)^2].

Table 1. Demographics and Baseline Clinical Characteristics in STR1VE-EU

Table 2. Primary and Secondary Results in STR1VE-EU

	onasemnogene abeparvovec 1.1 X 10^{14} vg/kg (N=32[a])	PNCR (N=23)
Independent sitting ≥10 seconds at any visit up to 18 months of age[b,c,d]		
n (%)	14 (43.8)	0 (0)
97.5% CI	26.4, 100	
p-value	<0.0001	
Event-free survival at 14 months of age[e,f]		
n (%)	31 (96.9)	6 (26.1)
95% CI	90.85, 100	8.14, 43.03
Difference from PNCR		
Difference	0.71	
SE Difference	0.10	
95% CI	0.48, 0.87	
p-value	<0.0001	

PNCR, Pediatric Neuromuscular Clinical Research. SE, standard error.
[a]33 patients treated, one patient dosed at 181 days and so was not included in the intention-to-treat population (N=32).
[b]A one-sided exact binomial test was used to test the null hypothesis of a p=0.1% at significance level of 0.025.
[c]The corresponding 97.5% confidence interval (CI) was estimated by the exact method for binomial percentages.
Milestone is confirmed by independent central review.
[d]vs. Pediatric Neuromuscular Clinical Research (PNCR) natural history data for SMA1 (N=23).
[e]Event-free survival at 14 months of age includes patients who did not die, did not require permanent ventilation, and did not withdraw from the study by 14 months of age.
[f]Exact 95% confidence interval (CI) and corresponding p-value calculated from a two-sided Fisher's exact test with a significance level of 0.05 for the comparison between onasemnogene abeparvovec and PNCR data.

Table 2. Primary and Secondary Results in STR1VE-EU

Conclusion: Despite some patients having more severe disease at baseline than those in the Phase III STR1VE-US study, STR1VE-EU final results demonstrated that the strong efficacy of onasemnogene abeparvovec reported in interim results was sustained. In addition, onasemnogene abeparvovec's safety profile remained consistent with the previously reported results.

Disclosure: The study was supported by Novartis Gene Therapies.

EPO-634

The Impact of Vulnerability on patients with Spinal Muscular Atrophy

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Background and aims: Vulnerability could be defined as the susceptibility and risk that contribute to having an increased possibility of being hurt physically, emotionally or mentally.
Methods: In a qualitative study previously carried out by FundAME, that followed a focus group methodology, and aimed to identify those aspects of the SMA that are most relevant to patients about their disease, vulnerability was identified as one of the 12 areas that have a high impact on patients and family members. Some patients and families expressed their concern about the risk of dying because of daily situations such as choking when swallowing or getting a serious respiratory infection after a minimal social exposure. Mainly three areas of vulnerability were identified: risks during feeding, susceptibility to respiratory infections, and the risk of losing and not being able to regain a safe positioning. With a view of evaluating the impact on the quality of life of patients and the disease burden of this novel concept, vulnerability, FundAME has requested patients in their registry to answer a set of items and questionnaires. These set of items and questionnaires were designed by a panel of experts composed by neuropediatricians, physiatrists, physiotherapists, psychologists, and patient representatives.
Results: Currently, patients with SMA and/or their parents are responding to the vulnerability items and questionnaires
Conclusion: The results of this study will be presented at the seventh Congress of the EAN 2021.
Disclosure: Partial financial support for this project is provided by Roche and AveXis.

EPO-635

Evidence of increased used of CPMS platform after a tailored online training: the Italian EURO-NMD experience

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Background and aims: The European Reference Networks (ERNs) are virtual networks connecting healthcare providers across Europe to ease diagnosis and treatment of rare diseases affecting more than 30 million Europeans. The Clinical Patients Management System (CPMS) is a digital web-based clinical software used by healthcare professionals in ERNs to discuss patient cases through virtual panels and to make patients' data available for registries and databases in a secure way. A 12-month project funded by Sarepta Therapeutics was set up to improve the use of the CPMS among Euro-NMD ERN Italian members.
Methods: • Two medical doctors (MD) underwent a teaching course with a CPMS expert to learn the platform use • The two o MD organized a training course across four months, with six lessons per month, with a flexible schedule to ease the course attendance.
Results: • 13 of the 15 Italian healthcare providers (HCP) joined the course • 32 participating professionals learned to access the platform and became acquainted in using it • At the end of the course, the Italian members of the Euro-NMD ERN had opened 87 panels (85% of the total) • During the course, some panels were instrumental for diagnosis, and the Italian network strengthened.
Conclusion: Cross-border virtual consulting is an outstanding tool to improve the quality of health care provision. However, the steep learning curve to become proficient in using a digital system in a foreign language may discourage its use. We found that a training course tailored to healthcare professionals might boost the usability of the CPMS platform, increasing its impact to European health system.
Disclosure: Funding by Sarepta Therapeutics. Authors acknowledge the ERN Euro-NMD.

Movement disorders 4

EPO-636

Clinical features and survival of treatment with Levodopa-Carbidopa Intestinal Gel in Advanced Parkinson's Disease.

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Background and aims: Levodopa-Carbidopa Intestinal Gel (LCIG) has demonstrated efficacy in reducing levodopa-associated motor complications in patients with advanced Parkinson's disease (PD). We aim to analyze the clinical characteristics and duration of treatment with LCIG in a cohort of patients with PD.

Methods: Observational study in patients treated with LCIG between January/2010-December/2019. Clinical and treatment variables were obtained. A descriptive and survival analysis was performed.

Results: 33 patients were included; 22 (66.7%) were women, with a mean age of 69.97 years (SD±9.6). 66.7% had non-tremoric PD. The time from onset of PD to start of LCIG was 13.82 years (SD±7.68). The mean dose of oral L-dopa prior to LCIG was 910.23mg/day (SD±223.11). The mean dose of LCIG was 1,323.19mg/day (SD±380.99), with a median of two extra doses/day (IQR: 2–4). After starting LCIG, 97% experienced improvement in OFF time and UPDRS-III score (Figure 1), 39.4% improved dyskinesias and 27.3% improved falls. 6.1% presented de novo impulse-control disorder and 36.4% had weight loss. 66.7% had gastrointestinal or device complications. Fifteen patients (45.5%) discontinued LCIG, 69.2% of them due to insufficient control of motor fluctuations. The Kaplan-Meier curve showed a median survival time of the LCIG of 51 months (95%-CI:30.01-71.99) (Figure 2). Patients with previous falls had lower drug survival (p=0.03) (Figure 2).

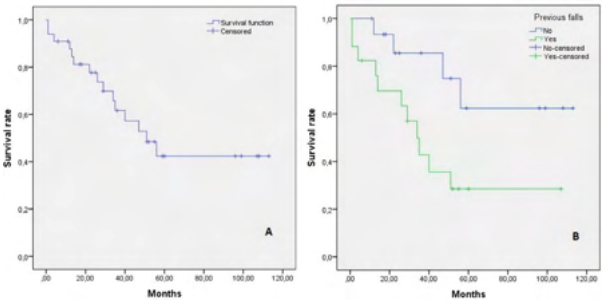

Figure 1. Comparison of median OFF time (A) and UPDRS-III score (B) during follow-up.

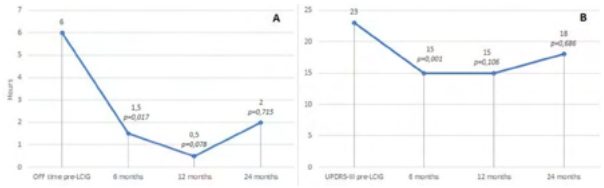

Figure 2. Survival curve of patients treated with LCIG (A) and comparison of survival curves according to the presence of falls prior to treatment (B).

Conclusion: LCIG is a therapy with a good initial clinical response and duration. Previous falls were associated with a shorter duration of this treatment. However, we found a significant percentage of withdrawal, mainly due to insufficient control of motor fluctuations and digestive complications during follow-up.

Disclosure: Nothing to disclose.

EPO-637

Clinical Trial Digital Endpoint Development: Patient & Provider Perspectives on Most Impactful Functional Aspects of PD

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Background and aims: Typically, Parkinson's disease (PD) clinical outcomes are evaluated via periodic, in-clinic visits. To assess PD more frequently, objectively, and from the patient's home using digital technology, Sanofi is developing the PD Functional Impacts Digital Instrument (PD-FIDI). Here we summarize the PD-FIDI's content validity research conducted to identify the most impactful everyday aspects of PD.

ethods: The research included a review of two clinician-recommended patient perspectives articles, concept elicitation interviews with 20 patients (5, idiopathic PD; 15, PD with glucocerebrosidase gene mutations), an online survey of 202 patients with PD, and two advisory board meetings with clinical experts. The meaningfulness of PD symptoms was rated as 'low', 'medium', or 'high', based on a comprehensive evaluation of this research.

Results: According to research articles, patients with PD prioritise improving a variety of motor and non-motor symptoms. In patient interviews and surveys, highly meaningful symptoms included difficulties with balance and gait, global motor function, rigidity/stiffness, tremor, depression, and fatigue (Table). Clinicians considered balance and gait, rigidity, and tremor-related hand and global motor functionality difficulties as highly meaningful, and also ranked depression and fatigue as pertinent (Table).

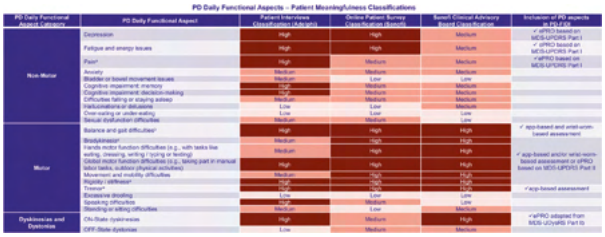

Table. Meaningfulness classifications of individual PD symptoms and functional impacts rated by interviewed patients, surveyed patients and clinical experts.

Conclusion: For both patients and clinicians, a subset of motor and nonmotor symptoms was identified as highly relevant for potential inclusion in the PD-FIDI. These insights were incorporated into the PD-FIDI's design where technically and operationally feasible (Figure). Additional qualitative evidence of content validity, as well as psychometric analyses examining the reliability, responsiveness, and usability of the PD-FIDI, will be evaluated in a yearlong clinical validation study.

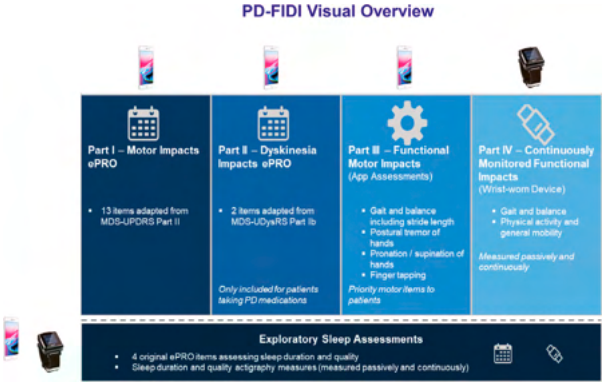

Figure. A visual overview of the PD-FIDI digital assessment tool and its components.

Disclosure: Study support: Sanofi.

EPO-638

Effect of safinamide in depressive symptoms: a post-hoc analysis of SADNESS-PD study

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Background and aims: SADNESS-PD was a real-life, multicenter, retrospective study which showed improvement in Parkinson´s disease (PD) depression in patients treated with safinamide. However, depression is not a single condition but specific depressive symptoms differ in outcome and functional impact. Our aim is to assess the effect of safinamide in different depressive symptoms according to the Hamilton depression score of 17 items (HAMD-17).

Methods: We calculated 10 composite scores from HAMD-17: mood (item 1), anhedonia (item 7), weight/appetite (items 12+17), insomnia (items 4+5+6), psychomotor agitation/retardation (items 9), fatigue (items 7), guilt (item 2), cognition (item 8), ideation of death (item 3), fear (item 10), somatic symptoms (items 11+14). Data were compared from baseline at months 1 and 3 of follow-up (Student's t-test for paired data, $p<0.05$).

Results: n=82 (safinamide 50mg=26,8%, 100mg=73,2%). HAMD-17 (Baseline=19,49±4,03. Month 1=13,49±5,10, $p<0.001$. Month 3=12,22±5,48, $p<0.001$). mood (baseline=2,54±0,86. Month 1=1,71±0,95, $p<0.001$. Month 3=1,50±0,95, $p<0.001$), anhedonia (baseline=2,18±0,83. Month 1=1,62±0,96, $p<0.001$. Month 3=1,40±0,94, $p<0.05$), weight/appetite (baseline=1,26±1,06. Month 1=0,85±0,97, $p<0.001$. Month 3=0,80±1,00, $p<0.001$), insomnia (baseline=3,10±2,03. Month 1=2,03±1,77, $p<0.001$. Month 3=1,85±1,73, $p<0.001$), psychomotor agitation/retardation (baseline=0,73±0,92. Month 1=0,40±0,59, $p<0.001$. Month 3=0,40±0,58, $p<0.001$), fatigue (baseline=2,18±0,83. Month 1=1,62±0,96, $p<0.001$. Month 3=1,40±0,94, $p<0.001$), guilt (baseline=0,84±0,78. Month 1=0,63±0,70, $p<0.05$. Month 3=0,51±0,71, $p<0.001$), cognition (baseline=1,68±0,90. Month 1=1,22±0,83, $p<0.001$. Month 3=1,20±0,74, $p<0.001$), ideation of death (baseline=0,38±0,64. Month 1=0,26±0,57, $p<0.05$. Month 3=0,18±0,50, $p<0.001$), fear (baseline=1,96±0,9. Month 1=1,35±1,00, $p<0.001$. Month 3=1,16±0,95, $p<0.05$), somatic symptoms (baseline=1,93±1,21. Month 1=1,33±1,08, $p<0.001$. Month 3=1,24±1,03, $p<0.001$).

Conclusion: Safinamide improved a wide spectrum of PD depressive symptoms, including those considered more disabling (mood), refractory (motor retardation, insomnia, cognition) and risky (suicide)

Disclosure: This study has been funded by Zambon.

EPO-639

Effect of safinamide in motor symptoms and motor complications: a post-hoc analysis of SADNESS-PD study

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Background and aims: SADNESS-PD was a real-life, multicenter, retrospective study which assessed the effect of safinamide on depression and motor state in Parkinson's disease (PD). Our aim is to assess the effect of safinamide in different motor symptoms and motor complications according to the Unified Parkinson's Disease Rating Scale (UPDRS).

Methods: We calculated eight composite motor scores from UPDRS: rigidity (item 22), bradykinesia (items 19+23+24+25+26+31), tremor (items 14+15+16+20+21+29+23), gait (items 13+14+15+29), axial symptoms (items 5+7+18+27+28+30+"gait"), dyskinesia (items 32+33+34), early morning dystonia (EMD, item 35) and motor fluctuations (items 36+37+38+39). Data were compared from baseline at months 1 and 3 of follow-up (Student's t-test for paired data or Fisher's exact test, $p<0.05$).

Results: n=82 (safinamide 50mg=26,8%, 100mg=73,2%). Basal UPDRS, I=4.56±1.82, II=13.59±6.67, III=22.91±8.68, IV=3.51±2.83. Safinamide improved rigidity (baseline=1.57±0.73. Month 1=1.31±0.78, $p<0.05$. Month 3=1.30±0.78, $p<0.05$), bradykinesia (baseline=10.20±3.57. Month 1=8.83±4.13, $p<0.001$. Month 3=8.57±4.12, $p<0.001$), tremor (baseline=2.48±2.06. Month 1=1.98±1.62, $p<0.001$. Month 3=1.90±1.73, $p<0.001$), gait (baseline=4.13±2.33. Month 1=3.40±2.40, $p<0.001$. Month 3=3.32±2.39, $p<0.001$), axial symptoms (baseline=10.04±5.66. Month 1=8.41±5.58, $p<0.001$. Month 3=8.34±5.46, $p<0.001$), motor fluctuations (baseline=1.73±1.51. Month 1=1.40±1.34, $p<0.05$. Month 3=1.28±1.30, $p<0.001$) and EMD (19.5% of patients at baseline. Month 1=9%, $p<0.001$. Month 3=11%, $p<0.001$). However, safinamide did not improve dyskinesia (baseline=0.78±1.47. Month 1=0.64±1.33, $p=0.160$. Month 3=0.65±1.26, $p=0.160$).

Conclusion: Safinamide was useful for a wide spectrum of motor symptoms, with special interest in those usually most disabling and refractory, such as gait and axial symptoms. In motor complications, safinamide was helpful for motor fluctuations but not for dyskinesia. It is important to remark its effect in EMD, an unpleasant and not-always-easy-to-treat complication.

Disclosure: This study has been funded by Zambon.

EPO-640

Influence of lockdown due pandemia on mental health in patients with Parkinson`s disease

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Background and aims: Pandemia due to SARS-CoV-2 virus infection has force many world countries on lockdown that has negative impact on mental and physical health of the world population. Parkinson`s disease (PD) is neurodegenerative disease with many motor and nonmotor symptoms among who psychiatric symptoms are most common. We aim to evaluate difference in level of stress, anxiety, depression and mental disorders between PD patients and healthy control and to examine how social life influence on this symptoms in PD patients during pandemic lockdown.
Methods: PD patients and healthy control were survey for mental disorders using CORE-OM (Clinical Outcomes in Routine Evaluation) and for depression, anxyety and stress using DASS-21 scale. Data about age, sex, disease duration, and questions about social life were collected using self-made questionairre.
Results: 50 PD patients and 30 healthy control were evaluated. PD patients more often live in the countryside and exercise regulary. Healthy control reported higher level of stress (DASS-21) and greater impairment in the subjective well-being and risk subscales (CORE-OM). PD patients who had at least one visit per week had a lower degree of anxiety and depression as well as better results in the CORE-OM sum total and in the subscales functioning and problems. PD patients who went for walk in company have also better results in the CORE-om sum total and in subscales subjective well-being and problems.
Conclusion: The control group showed higher level of stress and more mental disorders. More socialy active PD patients have lower degree of anxiety and depression and less mental disorders.
Disclosure: Nothing to disclose.

EPO-641

Motor and non-motor fluctuations in men and women citizen Uzbekistan with Parkinson's disease

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Background and aims: To identify the frequency and characteristics of the motor and non-motor fluctuations in men and women citizen Uzbekistan with Parkinson's disease (PD) and to establish their impact on the quality of life of patients.
Methods: We examined 42 men and 56 women with PD stages 2.5–4.0. The degree of clinical manifestations was determined using the Unified Parkinson's Disease Rating Scale and the Hoehn and Yahr scale. The 9-Symptom Questionnaire (patient self-assessment diary) was used to assess fluctuations. Quality of life was assessed using Parkinson's Disease Quality of Life Questionnaire 39 and the second part of the European Quality of Life Questionnaire.
Results: Among motor fluctuations, the on-off phenomenon prevailed, which occurred in 69.8% of men and 73.7% of women. Vegetative fluctuations were observed in 86.0% of men and 93.0% of women. Certain autonomic disorders were found statistically significantly more often in women than in men. Mental fluctuations were found in 79.1% of men and 75.4% of women. Apathy was recorded statistically significantly more often in men than in women. Among sensory fluctuations observed in 55.8% of men and 50.9% of women, pain syndrome was statistically significantly more common in women.
Conclusion: Gender influences the prevalence of certain non-motor fluctuations in PD patients.
Disclosure: Nothing to disclose.

EPO-642

NS-PARK/FCRIN network: the French research network on PD and movement disorders

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Background and aims: The French Clinical Research Infrastructure network FCRIN is a national clinical research infrastructure funded by the French government to boost clinical research in France. FCRIN funds investigation networks, including NS-PARK which brings together 26 French Expert Centers for Parkinson's disease (PD), with special focus on early interventional trials and large multicenter trials. This work will describe the organization and activities of NS-PARK/FCRIN network over the period 2015–2019.

Methods: Quantitative and qualitative indicators of activity are collected according to pre-specified outcomes elaborated by FCRIN and updated each year.

Results: NS-PARK has an efficient organization, based on an executive board and a steering committee, supported by four coordination managers and a sustainable business model. It gathers top scientific and methodological expertise to develop and conduct clinical trials, providing a single access to its centers, common recruitment strategies, harmonized costs, standardized quality system, training and access to research facilities. NS-PARK implemented a national cohort of PD patients (25,000 patients prospectively followed-up using a common clinical eCRF) and is developing its biobank and imaging database. From 2015 to 2019, NS-PARK conducted 50 projects among which 50% of NS-PARK projects were international studies and collaborated with 30 different industrial companies. 36% of NS-PARK project were funded by academic entities [European or national grants]. More than 2,800 patients were included.

Conclusion: NS-PARK is an efficient structure than improves clinical research in PD in France. Its objectives for the next years are to integrate clinical, biological, imaging and health care data analyses to develop personalized approaches of PD management.

Disclosure: The authors report no disclosure.

EPO-643

1-year follow-up of subthalamic stimulation in Parkinson disease: neurodegeneration and motor/non-motor outcomes

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Background and aims: The aim of the present study was to assess the short-term clinical and non-clinical impact of deep brain stimulation of the subthalamic nucleus (STN-DBS) in patients with Parkinson disease (PD).

Methods: Seven non-demented patients (5 males) with advanced PD were assessed before surgery and at 1-year (mean: 11,7 months) after continuous DBS treatment. All patients underwent a full clinical evaluation, a comprehensive neurocognitive assessment, and a serum neurofilament light (sNfL) levels testing.

Results: Comparing ON states pre-surgery and ON (medication-DBS) states post-surgery, walking and balance, motor aspects of activities of daily living (ADLs), as well as motor examination and complications significantly improved at one-year of STN-DBS. Moreover, quality-of-life aspects measured by Parkinson's Disease Questionnaire (PDQ-39) also improved, particularly for PDQ-39 mobility and pain subscales. No differences were found between baseline and one-year with regard to most of the neuropsychiatric domains assessed. However, although no major changes in global cognitive functioning were observed, a clear improvement in verbal intellectual scores were, however, found at one year. Remarkably, sNfL significantly decreased during follow-up for all patients.

Conclusion: In addition to the robust clinical effects in PD, STN-DBS also produces short-term improvements on ADLs and different domains of quality of life, as well as a general verbal intellectual improvement. The notable reduction of sNfL, a marker of neurodegeneration and neuroaxonal damage, could represent a transient neuroprotective effect of the DBS, likely caused by a dopaminergic-mediated "regulation" of STN stimulation.

Disclosure: This study was funded by Andalusian-Spanish PI-0025-2017, PI-0034-2019 and PSI2017-85951-R grants.

EPO-644

Disease Severity in the DUOGLOBE Patient Population Based on MANAGE-PD Section 2 Domains: Interim Subgroup Analysis

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Background and aims: DUOGLOBE is an ongoing global, observational study assessing long-term effectiveness of levodopa-carbidopa intestinal gel (LCIG) in advanced Parkinson's disease (APD) patients (NCT02611713). This post-hoc analysis assessed disease burden among subgroups of DUOGLOBE patients based on the frequency/severity of symptoms in the domains of Section 2 of MANAGE-PD, a clinician-reported screening tool to identify APD patients uncontrolled on oral/transdermal medications.
Methods: MANAGE-PD Section 2 domains were applied at baseline to DUOGLOBE patients. Patients were grouped by 1+, 3+, or six affected domains. Domains include Off time, troublesome dyskinesias, freezing of gait during Off time, falls, ADL impairment, and hallucination/psychosis. Efficacy and safety outcomes (Table 1) were evaluated at baseline and for mean change from baseline to Month 24 (M24).
Results: Of 176 patients with available Section 2 responses, 94.3%, 42.6%, and 1.7% had high enough frequency/severity in 1+, 3+ or 6 Section 2 domains, respectively. For patients with 1+ or 3+ affected domains, all efficacy outcomes improved from baseline to M24 except UPDRS II. Patients with more domains affected demonstrated greater numerical improvement. AE incidences were similar across groups.

Table 1. Mean Change from Baseline to Month 24 for Affected MANAGE-PD Section 2 Domains in DUOGLOBE Patients

Characteristic	1+ Domains		3+ Domains		6 Domains	
	Change from Baseline to 24 months mean ± SD		Change from Baseline to 24 months mean ± SD		Change from Baseline to 24 months mean ± SD	
	n		n		n	
OFF time	100	-3.8 ± 3.23	43	-4.6 ± 3.3	2	-8.5 ± 2.12
UDYSRS	85	-9.3 ± 21.97	37	-12.4 ± 21.06	1	-9.0 ± 0
NMSS	100	-24.4 ± 43.7	43	-28.1 ± 51.88	2	-56 ± 117.38
UPDRS II	106	2.4 ± 8.35	44	0.1 ± 8.64	2	-2.0 ± 4.24
PDQ-8	102	-6.3 ± 22.83	42	-7.7 ± 23.28	2	4.7 ± 6.63
MCSI	70	-2.7 ± 7.61	33	-4.0 ± 8.33	2	-1.5 ± 2.12

Patients were grouped based number of affected domains of MANAGE-PD section 2. APD = advanced Parkinson's Disease; LCIG= levodopa carbidopa intestinal gel; SD = standard deviation; UDysRS = Unified Dyskinesia Rating Scale; NMSS = Non-motor Symptoms Scale; UPDRS II = Unified Parkinson's Disease Rating Scale; PDQ-8 = Parkinson's Disease Questionnaire-8; MCSI= Modified Caregiver Strain Index.

Table 1. Mean Change from Baseline to Month 24 for Affected MANAGE-PD Section 2 Domains in DUOGLOBE Patients

Conclusion: A high percentage of patients demonstrated frequent/severe enough symptoms in at least one MANAGE-PD Section 2 domain at baseline prior to LCIG, indicating insufficient symptom control. At M24 all groups showed improvements in key outcome measures. The subgroups with 3+ and 6 domains have higher disease severity; however, only one affected domain of MANAGE-PD Section 2 is required to consider
device-aided therapy. Safety data were consistent with the profiles from phase three trials.
Disclosure: This study was funded by AbbVie Inc. AbbVie Inc. participated in the study design; study research; collection, analysis, and interpretation of data; and writing, reviewing, and approving this abstract for submission.

EPO-645

Use of the directional system in deep brain stimulation for post-surgical complications in Parkinson´s disease patients

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Background and aims: It is common to make adjustments in stimulation parameters after deep brain stimulation (DBS) in patients with Parkinson´s disease (PD) to improve parkinsonian symptoms and reduce adverse effects (AE) associated with stimulation. However, sometimes this setting is not enough to reduce these AE. We report three patients in whom post-surgical complications have been improved with directional system.
Methods: Three patients with PD of less than eight years of evolution were included. Patient 1 was treated with equivalent dose of levodopa (EDL) of 1, 000mg/day. Patient 2 had disabling cervical dyskinesia associated with levodopa and the EDL was 610mg/day. Finally, the EDL of patient three was 1,554mg/day. Subthalamic nucleus (STN) DBS was considered in all of them.
Results: Some adjustments in stimulation parameters were made after DBS. Parkinsonian symptoms were improved with increased stimulation intensity but AE appeared. Patients 1 and 3 had muscle stiffness that made it difficult to walk without having bradykinesia or tremor. Patient 2 had cervical dystonic dyskinesia that did not improve by reducing the stimulus duration. In all patients, the STN stimulus was directed towards dorsomedial, avoiding stimulating the internal capsule, with a clear improvement of these complications and the benefit on parkinsonian symptoms was maintained.
Conclusion: The directional system in DBS provides greater precision in stimulating motor region of STN avoiding nearby structures that cause AE.
Disclosure: All authors report no disclosures.

EPO-646

Deformation of the vertebral column in spastic hyperkinetic syndrome

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Background and aims: Nowadays, the scientific literature contains data on the possible development of secondary scoliosis in spastic torticollis. At the same time, almost no research has focused exclusively on the assessment of deformation of vertebral column in cervical dystonia.
Methods: The study included 50 patients aged from 27 to 81 with a diagnosis of spastic torticollis. All patients received regular botulinum toxin injections (at least three). All patients were assessed for the severity of cervical dystonia using the TWSTRS (Toronto Western Spasmodic Torticollis Rating Scale) and Tsui scales. All patients had their scoliotic angle measured with a manual goniometer using the Cobb method.
Results: Among the 50 patients studied, women predominated in a ratio of approximately 2:1. 72% of patients had left-side curvature of the neck and head, while the remaining 28% had right-side curvature. All patients included in the study were diagnosed with thoracic spine scoliosis. In 86% of cases the bulge of the scoliosis arch had the same direction as the displacement of the head. In 100% of cases the scoliosis arch was directed to the shoulder lift. We also found a close to logarithmic relationship between the values of the Cobb scoliotic angle and the severity of the condition of patients.
Conclusion: According to the received data, the assessment of deformation of vertebral column can be used as one of the methods for further examination and determining the severity of the condition of patients with cervical dystonia.
Disclosure: Nothing to disclose.

EPO-647

Possibilities of treatment of anxiety disorders in patients with blepharospasm

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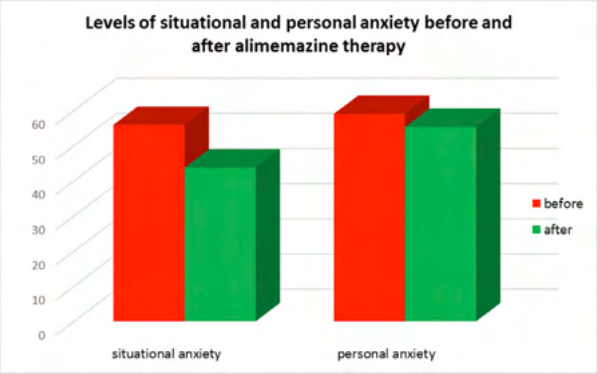
Background and aims: Blepharospasm is an involuntary contraction of the circular muscle of the eye, leading to persistent spasmodic closing of the eyelids. At the same time, the anxiety disorders associated with this pathology are not often taken into account by treating doctors.
Methods: The study included 28 patients with an established diagnosis of focal dystonia (blepharospasm) receiving botulinum toxin therapy and alimemazine therapy. All patients were evaluated for the severity and frequency of blepharospasm using the Jankovic Rating Scale (JRS). We also evaluated the initial level of anxiety before and after 30 days of therapy on the State-Trait Anxiety Inventory of situational and personal anxiety. Differences between the groups were considered significant at p<=0.05.
Results: In the initial assessment of blepharospasm on the JRS, the average level was 5.3±2.2, whereas after complex therapy it was 4.6±2.1. The average level of situational anxiety in the primary assessment was distributed in the average (25%) and high (75%) ranges and amounted to 55.9 ±15.7 points. When assessing personal anxiety, the 78.6% respondents had a high level of anxiety, 17.9% had medium and 3.5% had low level. After the course of alimemazine therapy, the average level of situational anxiety decreased by 21.8 %, or 12.2 points, and amounted to 43.7±13.6 points. The level of personal anxiety during the observation period remained without significant changes.



Conclusion: Our analysis confirms a significant reduction in anxiety in patients with blepharospasm after alimemazine therapy.
Disclosure: Nothing to disclose.

EPO-648

Non-motor symptoms perception by patients with Parkinson's disease

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Background and aims: Parkinson's disease (PD) is a multisystemic neurodegenerative disorder, commonly known for its cardinal motor symptoms: bradykinesia, stiffness and tremor. Non-motor symptoms (NMS), despite being present in most patients with negative impact in their quality of life, are still insufficiently reported in Neurology consultation.
Methods: PD patients were recruited from Movement Disorders Consultation in our Hospital Center, during five months. Cognitive function (MMSE), disease severity (Hoehn & Yahr Scale), demographic and clinical data were assessed. Portuguese version items of the NMS-Quest were presented randomly to PD patients, with other symptoms that are not part of the disease, and they were asked to select which symptoms were part of PD.
Results: 79 patients were included, with mean age 67.2± 10.7 years and 57% being male. Mean disease duration was 10.8±8.8 years and average H&Y stage was 2.3±0.6. Patients recognized 54.9±21.7% of NMS presented, with cardiovascular symptoms (77.2±29.7%), cognitive symptoms (69.6±35.1%) and depression (66.5±40.6%) being the most recognized. Education over four years was associated with greater perception of sexual dysfunction symptoms (80.9±43.2%; p<0.001). The perception of remaining NMS did not differ significantly between genders, degrees of disease severity and motor symptoms (MDS-UPDRS-III). Patients reported they learned about NMS with their Neurologist in 84.6% and in Primary Health Care in 16.7%.

Table 1. Demographics of Study Population	
Patients (n)	79
Male Gender (%)	57%
Mean Age (years, SD)	67,2 ± 10,7
Mean Disease Duration (years, SD)	10,8 ± 8,8
Mean H&Y Stage (n, SD)	2.3 ± 0.6

Demographics of Study Population

Table 2. Perception of NMS (%, SD)	
Cardiovascular	77,22% (29,74)
Apathy; Atention; Memory	69,62% (35,08)
Urinary	68,99% (36,96)
Depression; Anxiety	66,46% (40,60)
Sexual Disfunction	61,39% (42,33)
Hallucinations	49,37% (44,93)
Miscellaneous (pain; diplopia; weight loss)	45,13% (31,16)

Perception of NMS

Conclusion: Almost half of NMS were not recognized by patients with PD. It is essential to educate patients about their disease, in the Neurology consultation and in primary health care, to optimize the management of these patients.
Disclosure: Authors have no conflict of interest to declare.

EPO-649

Long-term efficacy of opicapone in reducing ON-time troublesome dyskinesia in patients reporting troublesome dyskinesia

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Background and aims: Opicapone (OPC) was shown to be effective for end-of-dose motor-fluctuations in PD patients [1,2].
Methods: Matching efficacy data was combined for OPC-50mg [1,2]. This post-hoc analysis evaluate the long-term effect of OPC on 'Bad ON-time' (ON-time with troublesome-dyskinesia) in OPC-50mg patients reporting troublesome-dyskinesia at baseline.
Results: 216 patients were included in Full-Analysis-Set. Of these, 44 (20.4%) reported ~2h of 'Bad ON-time' and ~9h of ON-time without/with non-troublesome-dyskinesia ('Good ON-time') at baseline. Following initiation of OPC-50mg and up to end of double-blind, an increase ~1.4h in 'Good ON-time' and decrease ~5mins in 'Bad ON-time' were observed, with a levodopa reduction ~40mg. By end of 1-year open-label, 'Good ON-time' increased ~2h and 'Bad ON-time' decreased ~1h. Levodopa decreased additional 60mg, ending in total decrease of 100mg.
Conclusion: In PD patients with motor-fluctuations and reporting troublesome-dyskinesia, OPC did not exacerbate troublesome-dyskinesia; in fact, long-term OPC-exposure and levodopa reduction, led to a relevant reduction of 'Bad ON-time' and increase ~2h of 'Good ON-time'.
Disclosure: 1.Ferreira et al., Lancet Neurol. 2016;15(2):154-165; 2.Lees et al., JAMA Neurol. 2017;74(2):197-206

Neurogenetics 2

EPO-650

SPG7 mutations in Hungarian cohorts: new insights and possible genotype-phenotype correlations

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Background and aims: Paraplegin encoded by SPG7 causes autosomal recessive hereditary spastic paraplegia (HSP). It is responsible for 5–12% of the HSPs. The SPG7 mutations result in pure HSP, but based on some observations the clinical picture can be more colourful.
Methods: We screened 342 Hungarian patients for damaging SPG7 rare variants (DRVs) by NGS. Based on phenotype 5 subcohort were established: spastic paraplegia; ataxia; motoneuron lesion; progressive external ophthalmoplegia, and patient with mitochondrial encephalopathy. We aimed to identify the frequency of the DRVs of the SPG7 in these patients and to compare its ratio in the subgroups.
Results: We identified 17 patients with biallelic, 16 patients with monoallelic DRVs. The p.Leu78Ter mutation was present in nine cases with biallelic, in four cases with monoallelic presentation. This DRV seems to be the most common DRV associated with HSP7 in Hungary. In patients with heterozygous presentation is seems to be disease-causing similarly as the p.Ala510Val mutation, which was proposed previously to be associated with HSP in heterozygous form as well. This latter was also common in the Hungarian cohort. The ratio of DRVs was the following in the subgroups: spasticity 11,39%, ataxia 17,61%, motoneuron lesion 7,87%, PEO 11,90%., and mitochondrial encephalopathy 9,64%.
Conclusion: SPG7 mutation result in wide clinical phenotype. The p.Leu78Ter DRV is the most common pathogenic mutation in Hungary beside the p.Ala510Val. Both of these DRVs may result in clinical signs both in monoallelic and biallelic form, the monoallelic alterations result in less severe phenotype.
Disclosure: The authors have nothing to declare.

EPO-651

Whole exome analysis in isolated population of Czech Republic with familial neurodegenerative parkinsonism

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Background and aims: Increased prevalence of neurodegenerative parkinsonism with familial aggregation has been described in an isolated region in the Czech Republic. The aim of the study was to identify genetic variants potentially associated with this disease using whole exome analysis.
Methods: NGS Ion AmpliSeq Exome method (IonTorrent) was used for five subfamily trios. Each trio comprised of two affected and one healthy person. DNA exome libraries were sequenced on IonPI chips. Variants were predicted using pipeline Torrent Suite/Ingenuity Variant Analysis/ Two case/control analysis. Final filtering was done with respect to population frequency (Global MAF1%), variant effects and biological context (Parkinsonism responsible genes). Last filter was done with respect to the segregation of the disease within particular subfamily.
Results: Each subfamily trio shows different set of suspected variants. Trio A shares two variants with trio D (novel variant NM_002386.3:c.322G>A;p.A108T in the gene MC1R/RP11-566K11.2 and rare variant NM_015210.3:c.1445C>T;p.A482V in the gene MTCL1), Trio B shares one rare variant with trio C (NM_001256864.1:c.1817A>C;p.H606P in the gene DNAJC6). In addition, in trios C and E there were found two novel gene CSMD1 variants NM_033225.5:c.3335A>G,p.E1112G and c.4071C>G; p.I1357M respectively.
Conclusion: It can be concluded that the genetic basis of this hereditary parkinsonism is likely to be heterogeneous. Assessment of the functional effect of these variants is ongoing. This study was supported by MH CZ – DRO (FNOl, 00098892, by the European regional Development Fund-Project ENOCH (No. CZ.02.1.01/0.0/0.0/16_019/0000868) and by IGA LF 2021-020.
Disclosure: Nothing to disclose.

EPO-652

Effect of the huntingtin gene repeats on the risk of depression in Parkinson's disease (PD)

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Background and aims: Huntington's disease (HD) patients are known to have a wide range of non-motor symptoms, and most of them have depression. Estimates of the prevalence of depression in HD vary widely, ranging from 9% to 63% [Jane S. Paulsen]. It is still not known to what extent the variation in the number of CAG repeats of the huntingtin (HTT) gene within the normal range can influence the risk of developing depression and its severity in another population of patients with movement disorders, including patients with PD. Objective was to assess the risk of depression in PD patients due to the variable number of CAG repeats of the HTT gene.
Methods: Materials: 160 patients with PD underwent neurological, neuropsychological (HADS, BDI-II, MoCA-test) and genetic examinations.
Results: The Random forest machine learning algorithm was used to classify clinical and genetic data. As a result of the study, a model was obtained that makes it possible to predict the development of depression depending on the number of CAG repeats of the HTT gene among patients with Parkinson's disease.
Conclusion: Thus, CAG repeats of the HTT gene in PD patients might be an underestimated factor in the development of depression. It is necessary to study this in a larger sample of patients in order to improve the possibilities for predicting the development of non-motor manifestations in patients with movement disorders and to understand the pathogenesis of the disease better.
Disclosure: Nothing to disclose.

EPO-653

Monocarbon metabolism disorders in Huntington's disease

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Background and aims: Several studies demonstrated that huntington's disease (HD) patients are hyperhomocysteinemic. This could be related to the role of huntingtin in the transsulfuration pathway, but also, to deficiencies in vitamin B12, B9 and B6. We hypothesize that an alteration of the carbon metabolism and the associated hyperhomocysteinemia may be aggravating risk factors for HD in terms of early onset and severity.
Methods: 36 patients followed at the Universitary Hospital of Nancy were included in the study between January and June 2020. We collected clinical (age of onset, UHDRS/disease duration ratio), genetic (CAG repeat number) and biochemical data (homocysteinemia, vitamin B6-B9-B12 dosages). We defined monocarbon metabolism disorders (MMD) by hyperhomocysteinemia (mol/L>15) or vitamin B6 (nmol/L<20), B9 (nmol/L<270) or B12 (pmol/L<150) deficiency.
Results: 14 HD patients presented monocarbon metabolism disorders (MMD+ patients) with a prevalence of 39% (9 hyperhomocysteinemias, three vitamin B12 deficiencies and four vitamin B6 deficiencies). Mean age of onset was lower in MMD+ patients than in MMD-patients (41,9±11,7 vs 47,4±11,0). Mean UHDRS/disease duration ratio was higher in MDD+patients than in MDD-patients (4,66±2,5 vs 3,16±2,37). However, mean CAG repeat number seemed similar in the two groups (44,5±3,52 vs 43,9±3,25).
Conclusion: MMD appear to be frequent in HD patients, with a prevalence of 39% in our study. MMD seem to be a marker of precocity and severity in HD and can contribute to phenotypic variability. Screening for vitamin B deficiencies and homocysteine status should be systematic in HD patients. Treating these disorders could improve HD patient's clinical condition and prognosis.
Disclosure: Nothing to disclose.

EPO-654

Pyramidal pathway changes at conventional brain 3T-MRI in patients with hereditary spastic paraplegia

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Background and aims: Conventional MRI can identify abnormalities associated with upper motor neuron (UMN) involvement. Motor cortex (MC) and cortico-spinal tract (CST) imaging abnormalities are reported in patients with amyotrophic lateral sclerosis (ALS), but their prevalence in other disease with UMN involvement is poorly studied. Our aim was to evaluate the occurrence of such changes in patients with hereditary spastic paraplegia (HSP).

Methods: We retrospectively evaluated 3T-MRI from 44 HSP (27 men, mean age 49.3±14.6), 55 ALS patients (35 men, 56.3±7.6) and 52 controls (34 men, 53.4±5.1). Features of interest were CCS T2/FLAIR hyperintensity, MC SWI hypointensity and selective MC atrophy. Differences among groups were tested using two or ANOVA based on data ($p<0.05$). We adjusted the analysis for age using logistic regression.

Results: HSP patients had more frequently CCS FLAIR hyperintensity than controls but less than ALS patients (40.5%, 30% and 67.3% respectively; $p<0.001$). The prevalence of MC SWI hypointensity (HSP 69.2%, ALS 73.5%, controls 18.8%; $p<0.001$) and atrophy (HSP 73.8%, ALS 64.2%, controls 42.3%; $p<0.01$) was similar in HSP and ALS patients, both higher than in controls. The results did not change adjusting for age.

Conclusion: The prevalence of MC and CCS MRI abnormalities in HSP patients was higher than in controls. However, it was similar to ALS patients, except for CCS FLAIR hyperintensity. less frequent in HSP, possibly reflecting pathophysiological differences. The finding of such MRI features support a pyramidal involvement but is not able to discriminate between HSP and ALS.

Disclosure: Nothing to disclose.

EPO-655

The role of MAPT haplotypes as a risk factors of frontotemporal dementia in a Russian cohort of patients

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Background and aims: It is known that H1 MAPT haplotype is a risk factor for some neurodegenerative diseases, such as progressive supranuclear palsy and corticobasal degeneration. One GWAS study revealed association between H1 MAPT haplotype and frontotemporal dementia (FTD), while other studies could not confirm this association.

Methods: SNP rs1800547 in exon 3 MAPT gene was used for haplotype verification (H1 or H2) by Sanger sequencing. The study sample consisted of FTD patients (n=42) and healthy controls (n=96). We investigated association between MAPT gene haplotypes and FTD in the general cohort, in subgroups of behavioral variant of FTD (bvFTD) and non-fluent variant of primary progressive aphasia (nfvPPA), and in patients with TDP43 pathology (9 carriers of mutations in GRN and C9orf72 genes).

Results: No differences were found between patient groups and control group on the evaluation of risk of alleles H1 and H2 for the development of FTD and its phenotypic variants (Table 1). We also found no risk of H1 and H2 haplotypes for the development of TDP43 pathology.

Group	H1, N (%)	H2, N (%)	P
general FTD	76 (90)	8 (10)	0.3524
nfvPPA	35 (92)	3 (8)	0.3443
bvFTD	35 (87)	5 (13)	0.8602
FTLD-TDP	17 (94)	1 (6)	0.3512
Control	166 (87)	26 (13)	-

Table 1. H1 and H2 MAPT haplotypes frequency in patients with FTD and control group

Conclusion: The absence of association between H1 and H2 haplotypes and the development of FTD in a Russian cohort of patient is consistent with the result of most studies in other populations.

Disclosure: The study was supported by RFBR grant #19-015-00533.

EPO-656

Novel splice-site and missense variant of PNPLA6 in an Austrian family causing spastic paraplegia-39

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Background and aims: Due to increasing awareness, broader usage and technical developments of genetic testing, novel neurological phenotypes due to mutations in specific genes with new complex genotype-phenotype correlations are being detected. Besides spastic paraplegia (SPG) 39, mutations of the PNPLA6 gene are associated with a wide spectrum of neurodegenerative diseases. We report a family with affected subjects suffering from a unique phenotype of SPG caused by novel mutations of PNPLA6 gene.
Methods: Five family members were affected by spastic gait and a cerebellar oculomotor disorder. Data from clinical, laboratory, electrophysiological testing and brain imaging were analyzed. Genetic analysis was done using next-generation sequencing. Segregation analyses were performed by Sanger sequencing. To assess the pathogenicity of genetic variants on the encoded protein, in silico assessments were carried out.
Results: Two hitherto unknown sequence variants in the PNPLA6 gene: a splice site variant c.1635+3G>T and a missense variant c.3401A>T, p.(Asp1134Val) were detected. Compound-heterozygous siblings presented with a novel clinical phenotype consisting of lower limb spasticity, a marked cerebellar oculomotor disorder and hypogonadotropic hypogonadism. Their homozygous paternal uncle presented with increased lower limb reflexes, an unstable gait and cerebellar oculomotor disorder. In silico assessments for structure and function of the protein will be presented.
Conclusion: PNPLA6 gene variants are associated with a broad phenotypic spectrum which can be expanded by upper motor neuron disorder, isolated oculomotor cerebellar dysfunction and a limited degree of hypogonadotropic hypogonadism. Our findings emphasize the complex role of PNPLA6 in different neuronal structures and its damage leads to neurodegenerative disorders.
Disclosure: The authors have no financial relationships and no conflicts of interest relevant to this article to disclose.

EPO-657

Determination of Pathogenesis-Related Common Gene Signature and Candidate Biomarkers in Parkinson's Disease

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Background and aims: Parkinson's disease is the second most common neurodegenerative disease. It is essential to clarify the pathways responsible for its complex pathomechanism for effective treatment. The aim of this study is to make inferences on the pathways for the pathomechanism of the disease and biomarkers by using expression profilling datasets.
Methods: In this study, three studies expression profilling data were analyzed by BrB arraytool.. The data included in the study were obtained from post-mortal substantia nigra, early stage blood, post-mortal "vagus: dorsal motor nucleus and inferior olivary nucleus" tissues. Differentially expressed genes were intersected with Venny tool and the relationship with disease was questioned with Webgestalt and KEGG tools.
Results: Analysis of three data sets revealed two common genes -RIOK3, TNS1-. When the blood tissue group is intersected with the 'substantia nigra' group, five different genes have been associated with the disease (PGCC, SNCA, ZNF24, PRKAco, SEPT8.
Conclusion: RIOK3 is one of the two genes identified in common in all three data sets, interacts with caspase 10 and regulates the NF-kappa B pathway activity. Inflammation induced by the NF-kappa B pathway and neurodegeneration in which caspases play a role have been discussed in the Parkinson's disease mechanism. SNCA is also resemble with alpha-synuclein that is main patological protein in Parkinso's Disease. These common genes and pathways detected in different data sets which include both early and late stage tissue samples, can illuminate the stage-independent pathomechanism of this complex disease, and may also be a guide for easily accessible biomarkers.
Disclosure: Nothing to disclose.

Neuroimmunology 2

EPO-658

Intermittent Fasting Affects Peripheral Neuroimmunology via Upregulating Serpina3n Signaling in Hindpaw Incision Model

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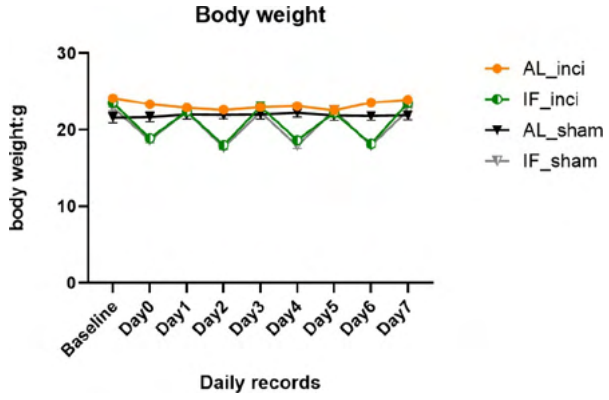
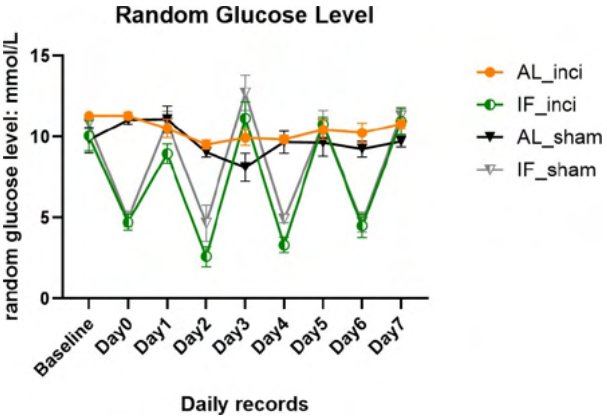
Background and aims: Neuro-inflammation acts as a inflammatory mechanism in neuro-immune activities. This study aims to investigate whether short-term intermittent fasting regulates basal metabolism and induces genetic changes to affect peripheral neuro-immunology in mouse hind-paw tissues after incision.

Methods: Hind-paw incision model was performed on mice. Body weight and random glucose level were recorded daily. Incised paw tissues were harvested before full recovery from surgery on two consecutive days of a complete fasting-and-refeeding cycle. mRNA levels of potential target genes were screened by qPCR and co-localization from protein levels was presented by immunofluorescent staining under confocal microscopy.

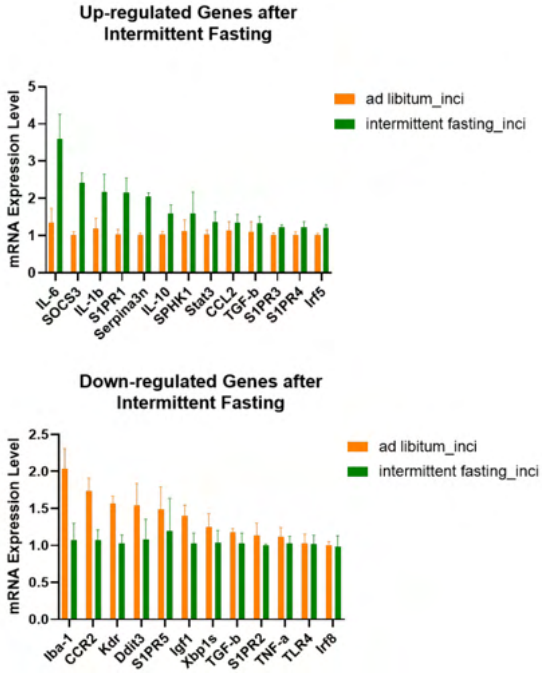
Results: Re-feeding does not induce hyperglycemia as mice lost weight during fasting and regained after re-feeding. qPCR has found that fasting alone could increase Serpina3n expression but decrease Iba-1 and CCR2 expression while re-feeding shrinks such effect in sham groups. Within incision groups, mRNA expression of IL-6, SOCS3 and Serpina3n were up-regulated while Iba-1 and CCR2 were down-regulated in mice under intermittent fasting compared with mice under ad libitum feeding. Interestingly, such difference seen in SOCS3 still exists even after re-feeding.



Mice lost weight during fasting and regained weight after re-feeding.



24-hour fasting will not induce hypoglyceamia and re-feeding after fasting does not lead to hyperglyceamia.



Compared to ad libitum group, mice under intermittent fasting have higher expressions of IL-6, SOCS3, IL-Ib, S1PR1 and Serpina3n ($p<0.05$), while lower expressions of Iba-1, CCR2 and Kdr ($p<0.05$).

Conclusion: Our findings suggest that short-term intermittent fasting is sufficient to alter genetic changes and thus affecting peripheral neuro-inflammation in mouse hind-paw tissues after incision, which might result from activating Serpina3n signaling during fasting. Though re-feeding tends to shrink fasting effects, potential molecular pathways involving upregulating SOCS3 or inhibiting Iba-1might still interact with neuro-immune activities during fasting. This study helps to provide new insights in understanding the mechanisms of fasting therapy and potential preventive strategy towards neuro-protection.

Disclosure: The study was supported by Department of Anaesthesiology, Li Ka Shing Faculty of Medicine, The University of Hong Kong.

EPO-659

Neurological complications of IgG4-related disease: experience from a tertiary center

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Background and aims: Neurological involvement in IgG4-related disease (IgG4-RD), although rare, is associated with well-defined syndromes. Its diagnosis can be challenging due to several clinical mimics, and nervous system biopsy inaccessibility, in some circumstances.
Methods: To characterize clinical, laboratory, neuroimaging and histological features of patients with IgG4-RD who develop neurological manifestations.
Results: 12 patients (6 females), with a median (IQR) age of 54 (23) years were included. 10 IgG4-RD were classified as "possible", one as "probable" and one as "definitive". The most common systemic involvement were asymptomatic lymphadenopathies. Neurological manifestations included meningoencephalitis (n=3, 1 with intracranial hypertension), meningomyelitis (n=3, two longitudinally extensive myelitis (LETM)), ganglionopathy (n=3, two dorsal root ganglionopathy and 1 Adie´s pupil), cranial neuropathies (n=2, one orbital pseudotumor syndrome), cerebellar syndrome (n=2), hemispheric dysfunction (n=1) and brainstem syndrome (n=1). Median (IQR) IgG4 concentration was 178 (86,3) mg/dL and 1,05 (0,9) mg/dL in serum and CSF, respectively. Seven (58%) patients had oligoclonal bands in CSF. Regarding MRI, the observed abnormalities were: white matter lesions (n=4, one multiple sclerosis-like), hypertrofic pachymeningitis (n=2), LETM (n=2), orbital pseudotumor (n=1), multiple cranial nerves hypersignal (n=1), middle cerebellar peduncles hypersignal (n=1), and diffuse leptomeningeal enhancement (n=1). Steroid-sparing agents included azathioprine (n=4), rituximab (n=2), cyclophosphamide (n=1), and hydroxychloroquine (n=1). Serum IgG4 concentration after corticosteroids beginning, decreased in all cases (n=6/6; median reduction (IQR) 33,9 (21,2) mg/dL).
Conclusion: : In our case series, we found neurological manifestations not previously reported in IgG4-RD: sensitive ganglionopathy and Adie´s pupil. The LETM and leptomeningeal involvement found in three patients are rare.
Disclosure: Nothing to disclose.

EPO-660

Prevalence of NMOSD in Central Serbia, 2020

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Background and aims: Population-based prevalence studies on neuromyelitis optica spectrum disorders (NMOSD) are limited. The aim of our study was to estimate the prevalence of NMOSD in Central Serbia, using the 2015 criteria.
Methods: In this population-based retrospective study, we included all patients from Central Serbia diagnosed with NMOSD according to the 2015 criteria. All those patients are included in the National NMOSD Registry of Central Serbia, established at the Clinic of Neurology, Clinical Center of Serbia in 2014. All tests for antibodies to aquaporin-4 (AQP-4) were performed in a single reference laboratory at the above-mentioned Clinic. Prevalence was calculated after re-evaluation of each patient according to the 2015 criteria on the day December 31, 2020. The projective number of inhabitants in Central Serbia (2019 projections) was 6,945,235 people, 3,383,732 males and 3,561,503 females.
Results: We identified 101 patients. There were 81 female and 20 male patients (4:1), with a median age at disease onset of 38 years (range, 7–68 years). In total, 90 % patients were positive for AQP-4 antibodies. Median Expanded Disability Status Scale score at the last visit was 3.0 (range 0–8.5). The prevalence was 1.45/100,000, for males 0.59/100,000, and for females 2.27/100,000.
Conclusion: Although, the prevalence increased in comparison with values assessed for NMOSD in Central Serbia in 2017 (0.98/100,000), based on the current prevalence data, NMOSD remains to be in the group of rare disorders. Having in mind these findings, continuous necessity exists to follow epidemiological parameters, such as markers of disease risk in our population.
Disclosure: Speaker honoraria: JD – BayerHealthCare, Sanofi-Genzyme, Medis, Merck, Roche; TP – Sanofi-Genzyme, Medis, Merck, Roche; SM – Medis, Merck, Roche; NV and OT – Medis, Merck, Novartis; VM, MA and JI – nothing to declare.

EPO-661

Dopamine modulates Th17-immune response via D2-like dopaminergic receptors in multiple sclerosis

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Background and aims: Dopamine participates in multiple sclerosis (MS) pathogenesis by modulating immune cell activity. This study aimed to clarify the role of dopaminergic receptors (DR) in dopamine-mediated modulation of Th17-cells in MS.

Methods: 34 MS patients and 23 controls were examined. The level of dopamine and homovanillic acid (HVA) in plasma and culture supernatants were determined by HPLC. To assess the effect of dopamine on Th17-cells, CD4+ T-cells were cultured in the presence of dopamine and stimulated with anti-CD3/anti-CD28-antibodies. The levels of IL-17 and GM-CSF in supernatants were assessed by ELISA. To study the involvement of DR in dopamine-mediated immunomodulation, CD4+ T-cells were pre-incubated with antagonist or agonist of DRD1 or DRD2, whereafter dopamine and anti-CD3/anti-CD28-antibodies or anti-CD3/anti-CD28-antibodies were added to the cultures.

Results: Dopamine and HVA plasma levels were lower in MS patients ($p<0.05$). The production of cytokines, dopamine, and HVA by CD4+ T-cells was comparable between the groups. Dopamine suppressed cytokine production in both groups ($p<0.0001$). Blockade of DRD1 had no influence on the inhibitory effect of dopamine, while blockade of DRD2 decreased dopamine-mediated suppression of IL-17 production in MS patients ($p<0.05$). Blockade of DRD1 suppressed cytokine production in both groups($p<0.05$), while DRD1-activation had no effect on cytokine production. Blockade of DRD2 had no effect on cytokine production, while DRD2-activation reduced cytokine production in both groups ($p<0.05$).

Conclusion: These data suggest an anti-inflammatory role for dopamine in MS, which could be mediated by the DRD2-activation.

Disclosure: This study was supported by grant from the Russian Science Foundation (project 19-75-00075).

EPO-662

Myelin oligodendrocyte glycoprotein antibody related disease following transverse myelitis due to ebv infection

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Background and aims: Differential diagnosis of transverse myelitis includes vascular,metabolic,inflammatory, infectious,neoplastic causes. We report a case of longitudinally extensive transverse myelitis (LETM) initially diagnosed as Epstein-Barr-virus(EBV)myelitis, three months later as myelin oligodendrocyte glycoprotein (MOG)-antibody-associated disease after brain stem attack.

Methods: A-32-years-old healthy-male presented with urinary retention,leg weakness, high fever, one week after upper respiratory tract infection.Neurological examination revealed asymmetric paraparesis, bilateral Babinski sign, hypoesthesia below T4, glob vesical.Magnetic resonance imaging (MRI) revealed longitudinal lesion in the spinal cord extending,contrast-enhancing between C5-7&T2-5 consistent with LETM (Figure-1). Brain MRI was normal. Cerebrospinal fluid (CSF) analysis showed 43 leukocytes, elevated protein levels.EBV-PCR was positive in the CSF. Oligoclonal band, aquaporin and MOG-antibodies were negative. Pulse steroid and antiviral therapy was administrated.Muscle strength returned to normal, urinary retention remained. Antibody tests for EBV revealed IgM:Negative,IgG:Positive (high avidity). After three months he was admitted with blurred vision and ataxia. Brain MRI showed diffuse hyperintense, enhancing lesion in pons (Figure-2). Repeated MOG-antibodies, which were assessed by commercial transfected fixed cell-based assay (Euroimmun,Germany) were positive this time. The patient recovered completely, was discharged with oral steroid and azathioprine treatment.

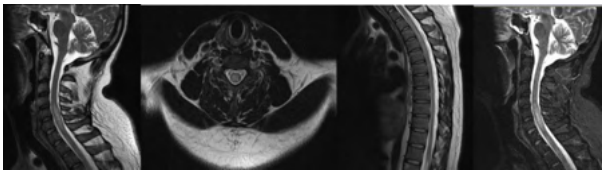

Figure-1

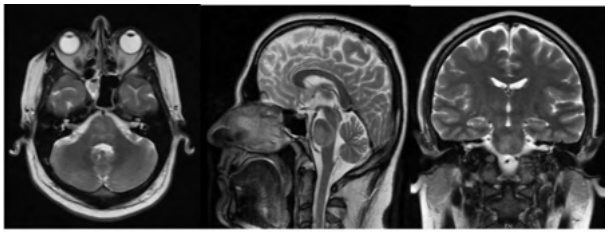

Figure-2

Results: Approximately six months later, the patient returned with numbness and loss of strength in the right leg and a feeling of tightness around the chest. Spinal MRI revealed a new lesion with minimal contrast enhancement above the previous lesion (Figure-3). The patient was treated with intravenous pulse methylprednisolone, his complaints almost completely disappeared. Oral steroid therapy dose was increased,a zathioprine treatment changed to rituximab.

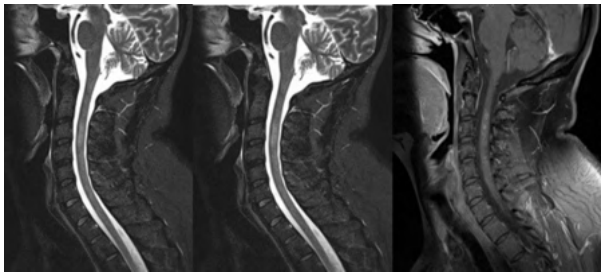

Figure-3

Conclusion: Our case report supports a relationship between MOG-antibodies and LETM which was triggered by EBV infection.MOG-antibody-associated-disease is a different entity than aquaporin-positive neuromyelitis optica spectrum diseases and should be considered in LETM when muscle weakness improves but sphincter functions are disproportionately impaired.
Disclosure: Nothing to disclose.

EPO-663

Encephalitis with positive GAD65 antibodies associated with a type I cryoglobulinemia and MGUS: a case report

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Background and aims: Encephalitis with positive GAD65 antibodies (Abs) is a rare and non-paraneoplastic autoimmune (AI) encephalitis. Its association with a type I cryoglobulinemia and monoclonal gammopathy of undetermined significance (MGUS) has not been reported in the literature. The aim of this study was to describe the particularity of clinical, diagnostic, therapeutic, and outcome features of a patient with encephalitis antiGAD65 Abs, regularly followed between November 2017 and July 2020.
Methods: Case report.
Results: We report the case of a 54-year-old woman who presented with progressive cerebellar ataxia, horizontal diplopia, dysphonia, dystonia of the right hand, psychomotor slowling and anxiodepressive syndrome. Brain magnetic resonance imaging and electroencephalography were normal. After an exhaustive biological assessment, antiGAD65 Abs were found significantly higher in cerebrospinal fluid and blood. The thoraco-abdomino-pelvic scanner and the Positron emission tomography did not find a cancer. A type I cryoglobulinemia associated with MGUS has been discorvered . Treatment with intraveinous Cyclophosphamide and Rituximab improved partially her AI encephalitis. The type I cryoglobulinemia and MGUS remained stable.
Conclusion: This is a case of non-paraneoplastic anti-GAD65 Abs encephalitis with an unusual clinical presentation. The discovery of type I cryoglobulinemia and MGUS associated with encephalitis antiGAD65 Abs is not fortuitous because they are autoimmune diseases. We have not found a similar case in the literature.
Disclosure: Nothing to disclose.We thank all actors involved in the care and monitoring of the patient described in this work in particular: “CH de Périgueux” , “CHU de Bordeaux”, “Centre de référence national pour les SNP et EAI (HCL-Lyon)”.

EPO-664

Seronegative autoimmune encephalitis presenting as a rapidly-progressive cognitive and movement disorder

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Background and aims: Subacute rapidly progressive behavioural and motor symptoms have a broad differential. Thorough clinical exploration, and laboratory and imaging findings are paramount to guide diagnosis and treatment.
Methods: Case report.
Results: A 57-year-old man with no relevant past medical history presented with five-week-long progressive mood and personality changes, visual hallucinations, gait impairment, daily recurrent vomiting, and weight loss, eventually becoming bed-bound. Neurological examination revealed disorientation, mixed aphasia, visual agnosia, amnesia, dysexecutive deficits, resting and postural tremor, bilateral parkinsonism, action and stimulus-sensitive myoclonus, and magnetic-like gait. Exhaustive investigation (blood tests, cerebrospinal fluid analysis, immunology and infectious panels, autoimmune antibodies, RT-QuIC, brain MRI, CT full body scan, whole-body PET) was unremarkable, except for raised protein levels (1.55g/L) in CSF. DaTSCAN disclosed dopaminergic deficits in the right striatum and left putamen. His condition progressed despite levodopa and rivastigmine therapeutic trials, and the initial diagnosis of Lewy body dementia was eventually deemed less probable. Notwithstanding the negative antineuronal antibody panel, a five-day course of iv methylprednisolone was tried. After seven days, the patient improved significantly, and oral steroids and mycophenolate were started. one year later, the patient is fully independent and remains symptom-free.
Conclusion: Seronegative autoimmune encephalitis is a challenging diagnosis. A high suspicion index is required, as adequate therapy may improve or even fully reverse symptoms and disability. We suggest that a therapeutic trial with corticosteroids should be considered in patients with rapidly progressive dementia whenever the etiology is not clear, although suggestive features (e.g. age, specific symptoms) warrant further research and clarification.
Disclosure: The authors declare no conflict of interest.

EPO-665

Effects of nano-resveratrol on mesenchymal stem cells derived from multiple sclerosis patients

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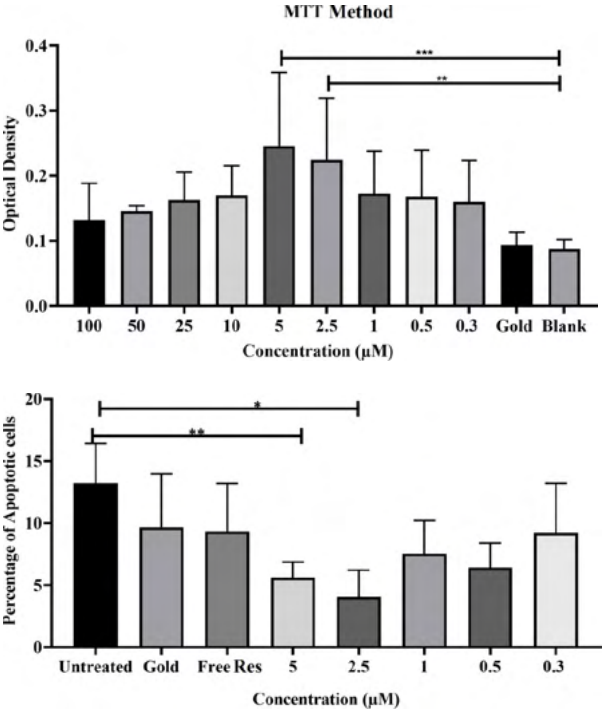
Background and aims: Multiple sclerosis (MS), the most prevalent neurological disability, is associated with central nervous system (CNS) lesions. Current therapies this autoimmune disease are not able to completely stop the destruction of nerve tissue. Mesenchymal stem cells (MSCs), as immunomodulatory agent, gained worldwide attention for MS. Besides, recently, resveratrol (trans-3,4',5 tryhidrostilbene), a natural polyphenolic phytoalexin from fruits and vegetables with multiple health benefits has attracted much attention due to its neuroprotective and anti-cancer and anti-inflammatory activities. However, poor bioavailability and water insolubility of resveratrol limited its clinical use while, the nano-formulations of resveratrol overcome these shortcomings. In the present study, we assessed comparative proliferation and anti-apoptotic effects of nano-resveratrol and its free form on adipose-derived MSCs from MS patients (AT-MSCs).
Methods: AT-MSCs was isolated form MS patient and characterized (immuno-phenotyping and conderogenetic and adipogenetic potential). Moreover, gold nanoparticles were synthesized and characterized. The percentage of proliferation and apoptotic death of MSCs were reported for nano-resveratrol and free resveratrol by MTT and flow cytometry methods.
Results: According to the data, the viability of MSCs significantly increased following exposure to nano-resveratrol (1.25, 2.5, 5 M, $p<0.001$). It also remarkably attenuated apoptosis in ATMSCs (2.5 and 5 M, $p<0.001$). Nano-resveratrol exhibited better proliferative and anti-apoptotic activities compared free resveratrol.



Conclusion: Considering our results suggested superior efficacy of nano-resveratrol on AT-MSCs to its free form. Hence, nano-resveratrol may considerate as complementary therapy for the MS patients who have received MSCs.
Disclosure: There is no conflict of interest.

EPO-666

Recurrent meningitis over nine years as the initial manifestation of Behçet disease

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Background and aims: Behçet disease (BD) is an inflammatory disease characterized by recurrent oral aphthous ulcers and numerous potential systemic manifestations. Neurological involvement usually occurs within the first five years of the disease, although neurologic findings precede non-neurologic features in only 3% of cases. Recurrent meningitis is extremely rare.

Methods: We present the case of a 45-year-old male who experienced three episodes of recurrent meningitis between 2011 and 2020. Each episode began with painful mouth sores followed days later by fever and progressive intense oppressive head pain. There was no evidence of other systemic involvement. Neurological examinations were normal, without meningeal signs. Cerebrospinal fluid (CSF) analysis revealed lymphocytic meningitis in every episode (Table 1).

Cerebrospinal fluid characteristics	July/2011	January /2013	September/2020
White blood cell count	124/uL (100% mononuclears)	120/uL (90% monnuclears)	350/uL (96% mononuclears)
Proteins	40 mg/dL	43 mg/dL	57 mg/dL
Glucose	58 mg/dL for 87 mg/dL blood glucose	72 mg/dL for 90 mg/dL blood glucose	66 mg/dL for 90 mg/dL blood glucose

Table 1. Cerebrospinal fluid characteristics during the outbreaks

Results: An extensive study was performed throughout the nine-year period, with repetitive negative serological tests, including VIH and syphilis. CSF Herpesviruses and Echovirus PCR analysis also tested negative in all three outbreaks. In 2020, the investigation was widened for autoimmune diseases, with negative autoantibodies and positive HLA B51 results. A cranial magnetic resonance showed a parietooccipital and cerebellar leptomeningeal enhancement. Our patient fulfilled O'Duffy-Goldstein criteria for incomplete BD and the International Criteria for Behçet's disease (ICBD) diagnostic criteria. Treatment with 1mg/kg/day prednisone was started. The patient was referred to a rheumatologist for immunosuppressive therapy.

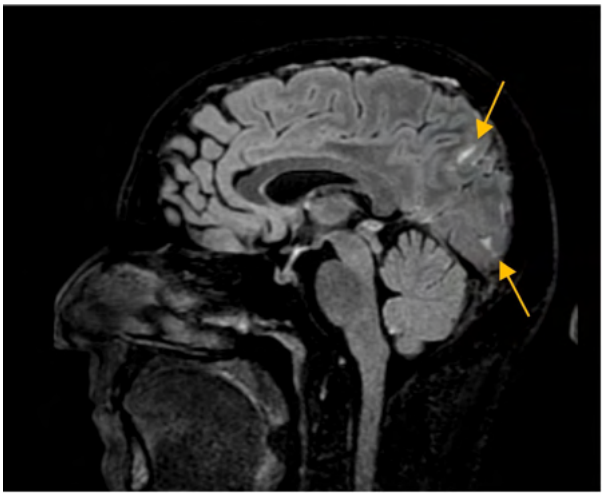

Figure 1. Sagittal T2 flair. Arrows pointing leptomeningeal enhancement

Conclusion: In patients with recurrent meningitis and negative results for the most common etiologies, BD should be considered in the differential diagnosis. Given its clinical presentation diversity, high diagnostic awareness is necessary to consider early treatment, to promptly suppress inflammatory exacerbations and recurrences to prevent irreversible organ damage.

Disclosure: The authors declare no conflicts of interest.

EPO-667

Downbeat nystagmus (DBN) as dominant manifestation of neurological syndrome with anti-GAD antibodies.

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Background and aims: Anti-GAD antibodies are described in stiff-person syndrome and other neurological syndromes, including cerebellar ataxia and epilepsy. DBN can be predominant feature of the clinical phenotype in the context of autoimmune or paraneoplastic anti-GAD neurological syndrome.
Methods: A 26-year-old woman with history of complex partial seizures of temporal origin with secondary generalization and paroxysmal episodes of gait instability and vertical nystagmus from the age of 23, presented with insidious onset and gradual progression of oscillopsia, ataxic gait with spasticity, multiple episodes of vomiting with subsequent weight loss and anxiety disorder.
Results: Neurological examination was remarkable for DBN in all gaze directions, proximal weakness of the left leg, spasticity with right preponderance and ataxic gait. Brain MRI and investigation for underlying malignancy were normal. EEG revealed epileptiform discharges in the frontotemporal areas of the right hemisphere. CSF analysis was consistent with chronic inflammatory response and type 2 oligoclonal bands. Anti-GAD antibodies were detected both in serum and CSF. The patient received intravenous methylprednisolone and underwent plasma exchange with amelioration of oscillopsia and left leg weakness, while DBN persisted. The patient achieved seizure freedom with briviracetam and recession of episodes of emesis. On follow-up the patient appeared stable with positive serum anti-GAD antibodies.
Conclusion: In patients with anti-GAD antibodies the diagnosis of epilepsy can precede that of cerebellar ataxia. DBN, either paroxysmal or permanent, can be a component of the clinical phenotype of great importance for the diagnosis of the anti-GAD neurological syndrome and should raise the suspicion for thorough investigation and prompt treatment initiation.
Disclosure: Nothing to disclose.

EPO-668

Sensitive axonal polyneuropathy in a patient with Recoverin antibodies and acute Rickettsia Conorii (RC) infection

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Background and aims: Several causes of polyneuropathy are known, being up to 20% immune mediated. In this group, axonal polyneuropathy account for a significant portion. In contrast to common causes of axonal polyneuropathy (as diabetes) immune-mediated polyneuropathy are often subacute and rapidly progressive, so rapid identification is imperative to target the treatment. Vasculitis, paraproteinemias or paraneoplastic syndromes should be ruled out.
Methods: A 41e-years-old woman without relevant medical or family history presented progressive distal limbs sensitive impairment and gait ataxia. Examination: lower limbs hypoesthesia, abolited reflexes and marked ataxia. She usually goes to the field but she denied previous fever or cutaneous rash.
Results: Neurophysiological study evidenced an intensive generalized axonal sensitive polyneuropathy. Blood test: positives IgM antibodies against RC and onconeuronal recoverin antibodies. Brain and spine MRI: normal. Body-CT and PET-CT: absence of malignancy. Ophthalmological study: no evidence of retinopathy. Normal lumbar puncture. She completed antimicrobial treatment and intravenous immunoglobulins with improvement.
Conclusion: In our patient there is a presumible acute RC infection (but without typical symptoms associated) and positivity to onconeuronal antibodies. Antirecoverin antibodies are mainly present in paraneoplasic retinopathy and optic neuropathy associated to small-cell lung or gynaecologic cancer. Involvement of peripheral nervous system after RC infection is extremely rare, mostly in form of demyelinating polyneuropathy. Axonal paraneoplastic polyneuropathy is more frequent, and often precedes the diagnosis of malignancy.
Disclosure: However, secondary to the prior explanations, it's important the close follow up being aware of possibility to develop a malignancy subsidiary to specific management.

EPO-669

2 cases of probable Neuro-Behçet's disease with longitudinally extensive transverse myelitis

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Background and aims: Neuro-Behçet's disease (NBD) with longitudinally extensive transverse myelitis (LETM) is not fully reported.
Methods: The clinical presentation and image studies of two patients with NBD with LETM were studied.
Results: Patient 1: A 52-year-old woman was admitted for progressive gait disturbance and hypoesthesia over three years. She had uveitis at the age of 49 and noticed recurrent oral ulcers. She showed muscle weakness of grade 4/5, hyporeflexia in lower limbs, and reduced deep sensation below T10. Spinal MRI demonstrated high signal intensity extending from the midbrain to the entire spinal cord on T2WI. Patient 2: A 44-year-old man was admitted for acute onset gait disturbance over six days. He showed muscle weakness of grade 0/5 affecting the lower limbs, hyperreflexia in upper limbs, reduced superficial and deep sensation on the limbs, and dysuria. Spinal MRI demonstrated high signal extending from Th2 to Th10 on T2WI. He had folliculitis and epididymitis. Two patients were treated with high-dose methylprednisolone. After the treatment HLA turned out B51 (Patient1) and B51 & A26 (Patient 2). Patient 2 was successfully treated with infliximab.
Conclusion: NBD with LETM is extremely rare. The present cases suggest that NBD should be considered as a differential diagnosis in patients with LETM.
Disclosure: Nothing to disclose.

Neurological manifestation of systemic diseases 2

EPO-670

Neurological Manifestations in Anti-Phospholipid Syndrome

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Background and aims: Antiphospholipid syndrome (APS) is a systemic autoimmune disorder defined by venous and/or arterial thrombosis and pregnancy morbidity in the presence of anti-phospholipid antibodies (aPL). Associated antibodies include anticardiolipin (aCL), lupus anticoagulant (LA), and anti-beta2-glycoprotein (anti-B2GPI) antibodies, found in 70%, 20% and 10% of patients, respectively. Neurological involvement is common and increases morbidity and mortality. We report two cases of APS presenting with different neurological manifestations.

Methods: The first case presented with acute ischaemic stroke causing right foot drop, with subsequent finding of multiple hypodensities on MR Brain. The patient was strongly positive for aCL and anti-B2GPI. An echocardiogram showed a valvular lesion highly suspicious of Libman-Sacks endocarditis. A diagnosis of APS was made and treatment with high dose steroids and rituximab were commenced. The second patient was previously diagnosed with APS and on therapeutic low molecular weight heparin for recurrent thrombotic episodes. She presented with right hemiparesis and neglect. CT revealed multiple haemorrhagic lesions in the left hemicranium with predominant subarachnoid distribution and associated oedema and mass effect. MR Brain showed extensive locules of subdural haemorrhage along the left concavity with evidence of blood layering within them and spillage into the subarachnoid space. MRA of the aorta showed mural inflammatory changes confirming large vessel vasculitis. Anticoagulation was stopped and treatment was initiated with a course of IV methylprednisolone followed by high dose oral prednisolone, hydroxychloroquine and rituximab.

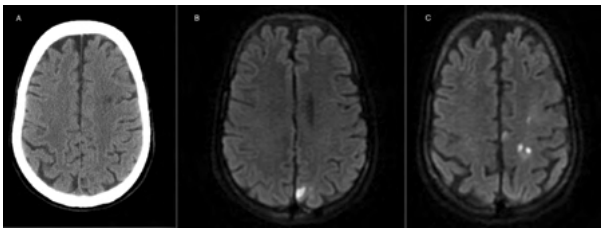

Figure 1 – Case 1: A: CT Brain showing small hypodensity in left frontal and parietal lobes; B, C: MR Brain DWI sequence showing multiple embolic infarcts

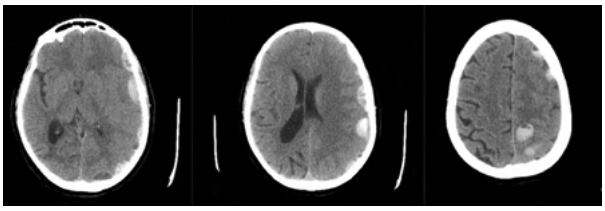

Figure 2 – Case 2: Axial CT images imaging showing multiple haemorrhagic lesions in the left hemicranium with predominant subarachnoid distribution and mass effect

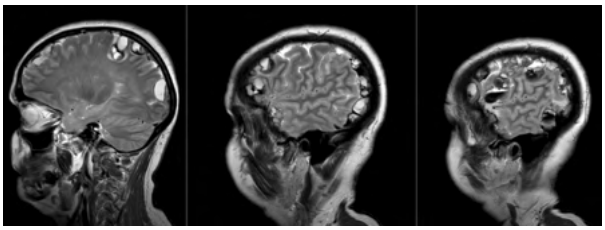

Figure 3 – Case 2: Sagittal T2 weighted MR images showing extensive locules of subdural haemorrhage along the left concavity with evidence of blood layering within them and spillage into the subarachnoid space

Conclusion: These cases highlight the wide spectrum of possible neurological sequelae that may be seen in association with APS.

Disclosure: Nothing to disclose.

EPO-671

A case of concomitant hyperosmolar hyperglycem ic state and autoimmune encephalitis.

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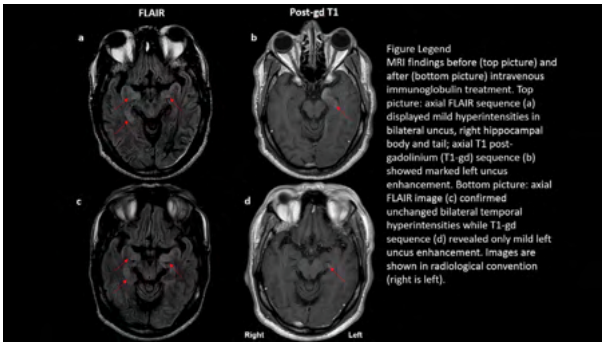
[1] Department of Neurology and INSPE, Milan, Italy, [2] Neurology and EPO112 Neurorehabilitation Unit Neuroimaging Research Unit Neurophysiology Service, Milano, Italy, [3] Neurology, Milano, Italy

Background and aims: Autoimmune encephalitis (AE) is an inflammatory disease of the brain, due to paraneoplastic and/or immune-mediated disorders. Differential diagnosis include infectious, toxic and dysmetabolic encephalitis/encephalopathies. Among the dysmetabolic encephalopathies, the hyperosmolar hyperglycemic state (HHS) can manifest in patients with type-2 diabetes as subacute encephalopathy.
Methods: Case Report
Results: A 49 year-old man with no previous medical history was referred to our hospital with a one-month history of general malaise, fatigue, progressive cognitive impairment and drowsiness. The patient appeared dehydrated confused, answering questions not properly with tendency to perseveration, having difficulty understanding simple commands. He had no meningeal or focal neurological signs. Serum blood glucose was 673mg/dl with preserved C-peptide. As he did not respond to the metabolic correction treatment, we performed further analysis such as magnetic resonance imaging (MRI), cerebrospinal fluid (CSF) and electroencephalography. MRI revealed bilateral temporal FLAIR hyperintensities involving bilateral uncus, right hippocampal body and tail. Left uncus demonstrated enhancement on post-gadolinium T1-weighted sequence. Electroencephalography showed two secondarily generalized seizures starting from left temporal focus. CSF showed mild pleocytosis (5 cells /μL). Screening panel for autoimmune and infectious aetiologies returned negative, with the exception of anti-GAD antibodies on serum (9.3U/ml range: 0–4.0U/ml), and on CSF (0.1U/ml). Collected data were suggestive of AE and the patient was successfully treated with intravenous immunoglobulin with clinical and neuroradiological recovery.



MRI scans

Conclusion: To the best of our knowledge, this is the first description of an association between AE and HHS. HHS metabolic and inflammatory storm may trigger autoimmune reaction and promote AE.
Disclosure: Nothing relevant to the present study.

EPO-672

Skull base inflammatory pseudotumor causing cranial multineuritis as a manifestation of IgG4 related disease

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Madrid, Spain

Background and aims: Inflammatory psexudotumor (IPT) in the head commonly involves the orbit, but it has been also described in other locations such as nasopharynx, skull base and brain parenchyma. The differential diagnosis is wide and includes lymphoma and other neoplasms.
Methods: We report a case of cranial multineuritis in a patient with a skull base IPT associated with IgG4.
Results: A 65-year-old man presented with progressive hearing loss, dysphonia and gait ataxia over the course of several months. A cranial MRI showed a mass involving the cavum and the skull base, with infiltration of both the dura mater and the internal auditory canals. A FDG-PET showed increased metabolism in the cavum, from where a first biopsy was taken, with normal results. Five months later, the patient developed a right sixth nerve palsy. A new MRI showed enlargement of the previous mass and CSF examination showed mild increment of leukocytes and proteins, with negative cultures and cytology. Despite the clinical deterioration, a second FDG-PET and cavum biopsy were normal. In a third biopsy, samples of the dura and petrous apex were taken through a transmastoid approach, which revealed an IPT with IgG4 deposits. After the diagnosis, the patient was initiated treatment with corticosteroids and rituximab, showing progressive clinical and radiological improvement.
Conclusion: IPT of the skull base is an infrequent manifestation of IgG4 related disease, and should be included in the differential diagnosis of other intracranial masses involving the skull base or meninges.
Disclosure: The authors declare no conflicts of interest.

EPO-673

Ataxia with central pontine myelinolysis (CPM) secondary to recurrent severe hypoglycemia

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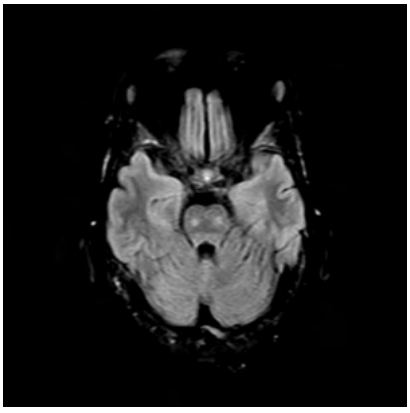
Background and aims: Cerebellar ataxia is a rarely reported complication of severe hypoglycemia, usually related with CPM, a central pons osmotic demyelinating lesion. The CPM etiology is diverse, more frequently related to rapid corrections of severe hyponatremia. However, it is also described in diseases resulting in rapid and significant shifts in plasma osmolality in absence of abnormalities of sodium homeostasis.
Methods: A 45-years-old woman, with diabetes type 1 and Graves-Basedow disease presented with abrupt speech disturbance, ataxia and impairment to swallow after a severe hypoglycemic episode (30mg/dl). She referred recurrent severe hypoglycemic episodes. Examination revealed slurred speech, upper and lower limbs dysmetria, weak left limbs reflexes, and a wide based unsteady gait ataxia with no Romberg's sign.
Results: Cerebral CT and extensive blood test were normal. Brain MRI showed a non contrast-enhancing central pontine lesion, hyperintense on T2 and FLAIR, and isointense on T1 sequences. A MRI after two months showed significant decrease in the lesion size. Few months later, only minimal residual neurological deficit with light unsteadiness on walking and slurr**Disclosure:** Nothing to disclose.ch persisted.



Conclusion: Neurological manifestations of hypoglycemia include behavioural change, confusion, loss of consciousness and seizures, but ataxia is unusual because cerebellum is protected by the glucose uptake. CPM secondary to hypoglycemia is a rare entity, associated with continued neurologic dysfunction, however, our case showed improvement despite the lesion. Proposed pathophysiology is a citotoxic edema secondary to impairment of the cellular ion pumps. Changes of blood glucose concentrations can be as brisk and profound as to cause significant serum tonicity changes leading to CPM.
Disclosure: Nothing to disclose.

EPO-674

Ictal visual hallucinations as a manifestation of hyperglycaemia

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Background and aims: Disorders of visual perception are uncommon manifestations of acute symptomatic seizures in the setting of hyperosmolar hyperglycaemic nonketotic syndrome (HHNK). These phenomena have been associated to typical MRI patterns, in particular to T2/FLAIR subcortical hypointensities. We report the case of a patient with HHNK, presenting with changing complex visual phenomena.

Results: A 64-year-old woman presented to the emergency department with a three-day history of left visual field defect and recurrent visual phenomena. The examination revealed left horizonto-rotatory nystagmus in primary gaze, persistent left homonymous hemianopsia and multiple episodes of left oculocephalic version, right-beating nystagmus and complex left-field visual hallucinations. These episodes lasted for about 20 seconds. At admission, the patient had a glycaemia level of 448mg/dL and glycated haemoglobin (A1c) was 11%. The electroencephalogram showed right temporo-occipital epileptic activity and brain MRI revealed a right parieto-occipital subcortical hypointensity with cortical hyperintensity in T2/FLAIR sequences. N-acetyl aspartate/creatinine ratio in spectroscopy was in the lower limit normal. The patient was treated with insulin, oral antidiabetic agents and levetiracetam, lacosamide, phenytoin and clonazepam. However, visual phenomena persisted and prosopometamorphopsias, transient complex visual hallucination, and hyperchromatopsias emerged progressively. Visual phenomena gradually resolved with glycaemic control, after two weeks of hospitalization. The patient was discharged with subcutaneous insulin, metformin and optimized antiepileptic treatment.

Conclusion: Hiperglycaemic states are sufficient conditions for development of acute symptomatic occipital seizures and typical MRI changes. During the period of uncontrolled glycaemia, visual phenomena can change over time, be refractory to antiepileptic drugs, and revert with correction of the metabolic insult.

Disclosure: Nothing to disclose.

EPO-675

The comprehensive evaluation of neurological complications of systemic diseases

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Background and aims: In evaluating the neurological complications of systemic diseases, peripheral nerves damage is rather assessed, but the central nervous system impairment is not considered. Our aim was to evaluate neurological complications of systemic diseases using the example of type 1 diabetes (T1D) and the differences between the patients who received various methods of insulin therapy in terms of development of cognitive decline and distal symmetric sensory polyneuropathy (DCCP).

Methods: We interviewed 100 people 29±11 years with T1D duration 14.25±9.25 years. The level of HbA1c was 9.5±1.5 %. The first group (n=50) were earlier on multiple daily insulin injections (MDII) for 11.3±5.4years and subsequently on continuous subcutaneous insulin infusion (CSII) for 4.5±1.5years. The second group (N=50) had MDII only for 12.7±7.7years. Assessed using Montreal Cognitive Assessment (MoCA), Trail making test (TMT), Words memorising test, Benton's similarity test, Neuropathy Symptoms Score (NSS), Neuropathy Disability Score (NDS), Total Symptoms Score (TSS).Statistical analysis was performed using Wilcoxon`s and t-test ($p<0.05$). Results are described by Median (Q25; Q75).

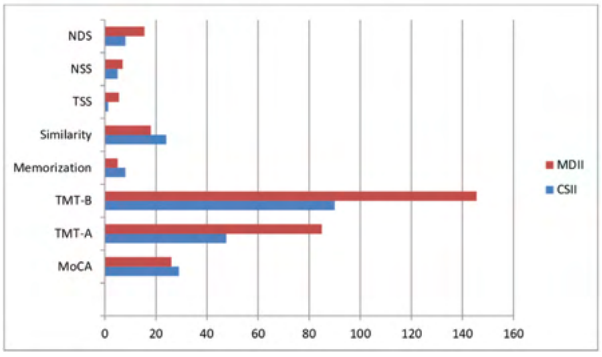
Results: The assessment showed lower scores for a decrease in cognitive functioning for the individuals in the the CSII-group vs MDII-group and higher scores in the MDII-group for DCCP (Table 1, Figure 1).

Table 1. Comparative results of the assessment of the studied groups

	CSII-group	MDII-group
MoCA	29 (28;30)*	26 (24;28)*
TMT-A	47.5 (38;65)*	85 (60; 96)*
TMT-B	90 (60;120)*	145.5 (115;180)*
Words memorising test	8 (6;8)*	5 (4;6)*
Benton's similarity test	24 (22;26)*	18 (16;23)*
TSS	1.3 (0;3.3)*	5.5 (4.7;7)*
NSS	5 (0;6)*	7 (6;8)*
NDS	8 (6;10)*	15.5 (14;23)*

*($p<0.05$)

Figure 1. Comparative results of the studied groups



Conclusion: Systemic diseases (T1D) may be complicated by the central and peripheral nervous system disturbances. In this group with T1D, severity of the complications in the MDII-group vs CSII-group was higher, and potentially linked in the method of insulin therapy. Comprehensive evaluation, including assessment of cognitive functioning, may benefit for understanding of the extent of neurological complications.

Disclosure: Nothing to disclose.

EPO-676

Hemorrhagic Stroke due to HELLP Syndrome, a case report

R. Simões Pissinatti [2], A. Da Silva César [1], P. Carvalho Batista [4], L. Mendes [5], E. Viegas Segundo [2], W. Botelho [1], A. Da Silva Dornelas [6], I. Paiva [3]

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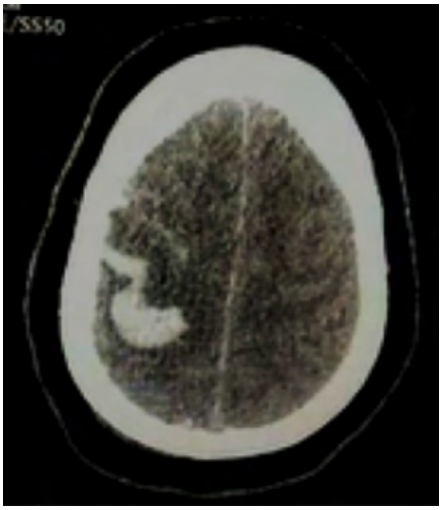
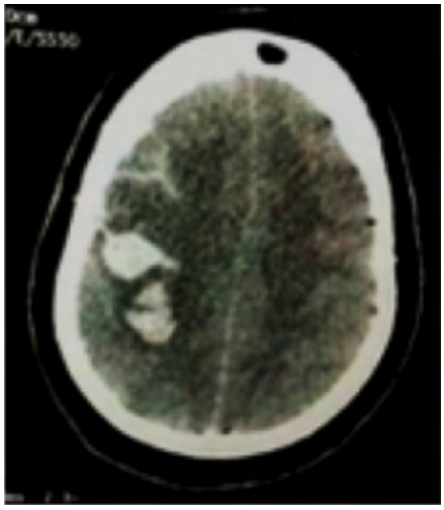
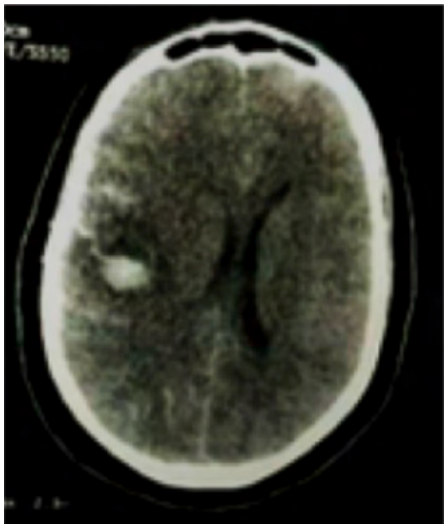
Background and aims: HELLP syndrome designates microangiopathic hemolysis, liver dysfunction and thrombocytopenia, which in Brazil has an incidence of around 12% and mortality of up to 24%, justified by systemic complications, with hemorrhagic stroke being the most common.

Methods: NGR., 35 years old, third pregnancy, 33 weeks and five days of gestation. Admitted to the Obstetric Emergency Room presenting headache, blood pressure 220/110 mmHg, vomiting, visual scotomas and anasarca. Previously healthy, irregular prenatal follow-up. Normal fetal heartbeat, absent uterine dynamics and dilated uterine cervix 3 cm. Submitted to emergency cesarean section, diagnosed with HELLP syndrome, she developed a lowered level of consciousness and seizure after delivery. Head computed tomography was performed, evidencing subarachnoid and right parietal intraparenchymal hemorrhage, with mass effect. It evolved with arreflex bilateral mydriasis, and brain death and organ donation protocols were performed.



Head computed tomography evidencing subarachnoid hemorrhage in the right cerebral hemisphere associated with right parietal intraparenchymal hemorrhage with mass effect; Fisher scale – grade 4.





Results: During pregnancy, changes in self-regulation and perfusion of cerebral vessels can trigger acute cerebrovascular complications. Maternal cerebral vasculature is highly vulnerable to the adverse effects of preeclampsia and HELLP Syndrome, a condition associated with increased risk of hemorrhagic stroke, responsible for high mortality in pregnant women. This scenario may be related to endothelial dysfunction, platelet activation, and altered vasorreactivity that together culminate in brain vasculature damage. However, this outcome may be reversible if early diagnosis and recognition of risk factors are performed.
Conclusion: Adequate gestational follow-up and management of risk factors are essential to reduce neurological complications and morbimortality from HELLP syndrome. It is also important to suspect stroke in patients with lowered level of consciousness after delivery.
Disclosure: Nothing to disclose.

EPO-677

Neurological manifestations of Primary Sjogren's Syndrome: a systematic review of the current literature

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Background and aims: Primary Sjogren's syndrome (pSS) is a chronic autoimmune inflammatory disorder primarily characterized by lacrimal and salivary gland dysfunction. In addition, it is associated with a complicated cluster of syndromes affecting the peripheral (PNS) and central (CNS) nervous system. The purpose of our systematic review was to determine the spectrum of neurological manifestations in pSS.
Methods: We conducted a literature search in PubMed using the search terms: Sjogren's or Sjogren AND 'Neurological or neuropathy or neuronopathy or nervous or ganglionopathy or ganglionitis or ataxia or autonomic or myopathy or myositis or myoclonus or palsy on 24/12/2019. Filters used were English, humans, full text.
Results: 60 papers were eligible to be included. In total, they provided data of 20,366 pSS patients diagnosed according to established diagnostic criteria (mean number of pSS patients per study was 351, median 85, range 11–6,331). The majority of the studies were on pSS patients with PNS manifestations. Polyneuropathy, which is mainly length-dependent or sensory ganglionopathy, is the most commonly studied, followed by autonomic dysfunction and single mononeuropathies (peripheral or cranial). The most frequent CNS manifestation in pSS patients is cerebellar ataxia, followed by cognitive dysfunction and headache. Few studies provided evidence that pSS is also associated with cerebrovascular incidents, seizure disorders, myositis and myelitis or other multiple sclerosis-like syndromes.
Conclusion: This review confirms that neurological manifestations are common in pSS patients. Evaluation of such patients in joint neuro-rheumatology clinics is highly recommended.
Disclosure: Nothing to disclose.

EPO-678

Peripheral nerve hyperexcitability syndrome associated with anti-Hu antibodies

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Background and aims: Paraneoplastic neurological syndromes (PNS) are mostly immune-mediated disorders. The neurological symptoms usually precede cancer diagnosis and its recognition usually leads to early cancer identification. Onconeuronal antibodies are found in 60% of PNS, with anti-Hu being one of the best described.
Methods: Case report.
Results: 60-year-old man, smoker, with a five-month history of lower limbs sensory loss and weakness with progression to inability to walk, urinary retention and significant weight loss. Neurological examination revealed dysarthria, spastic tetraparesis, action myoclonus of the limbs, fasciculations in the face, torso and limbs; loss of all sensory modalities below D6, appendicular and axial ataxia. Ancillary testing revealed cerebrospinal fluid (CSF) pleocytosis, IgG intrathecal synthesis and anti-Hu antibodies in both serum and CSF. The contrast brain and spine magnetic resonance imaging was normal; the electroencephalography showed generalized slow wave activity; the electroneuromyography revealed generalized spontaneous continuous muscular activity. The biopsy of a mediastinal lesion disclosed metastatic small cell lung cancer. Steroids and a cycle of intravenous human immunoglobulin was tried with incomplete response. Myoclonus attenuated with clonazepam. There was a rapid deterioration with pancerebellar syndrome with oculomotor apraxia, worsening of dysarthria and dysphagia, severe neuropathic pain, and cognitive deterioration, preventing the treatment of the primary tumour, ultimately leading to death after two months.
Conclusion: Most patients with PNS related to anti-Hu have multifocal neurological manifestations, most commonly encephalomyelitis or cerebellar degeneration, both present in this case. However, to the best of our knowledge the presence of peripheral nerve hyperexcitability syndrome has not been previously described.
Disclosure: Nothing to disclose.

EPO-679

Abstract withdrawn

Ageing and dementia 4

EPO-680

Effect of vitamin D supplementation on anxiety-depressive disorder at six months of stroke: a randomized clinical trial

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Background and aims: According to literature, stroke patients can suffer from mood disorders, which negatively affect the patient's daily functioning and quality of life. Through its influence on cytokine expression, vitamin D may be implicated in the development of anxiety-depressive disorder after stroke. The aim of this study is to determine the effect of vitamin D supplementation on anxiety-depressive disorder at six months of a first ischemic or hemorrhagic stroke.
Methods: This is an interventional study type. We included patients with a first ischemic or hemorrhagic stroke and suffering from vitamin D deficiency. The sample was randomized into two groups. One group received vitamin supplementation (600,000 IU vitamin D3 IM) with the conventional treatment protocol and the other group received the conventional treatment protocol only. The assessment of anxiety-depressive disorder took place at six months using the Hamilton Anxiety Rating Scale and Beck Depression Inventory-II.
Results: We included 147 patients. About 21 % of participants presented an anxiety and 51 % a depression. The proportion of patients suffering from this disorder was comparable between the two groups. We studied its effect according to age, gender, type of stroke, stroke severity and initial vitamin D status. Supplementation had a statistically significant benefit and reduced the occurrence of depression for younger subjects (30,4% vs 57,1%, OR=3.04 (95% CI, [0.95–-9.73], p=0.04)).
Conclusion: Vitamin D supplementation may have provided some protection for certain subgroups. Optimization of the supplementation protocol may offer more encouraging results.
Disclosure: Nothing to disclose.

EPO-681

Intracranial dural arteriovenous fistula presenting as progressive dementia and parkinsonism

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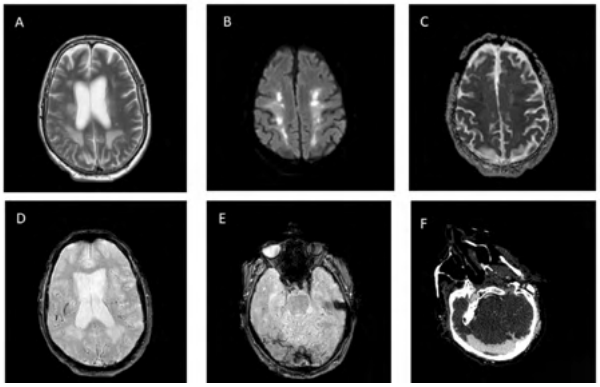
[1] Neurology department of Hospital Principe de Asturias, Madrid, Spain, [2] Neurology, Madrid, Spain, [3] Neurology, Alcalá de Henares, Spain

Background and aims: Dural arteriovenous fistula (DAVF) is a rare, but potentially treatable neurological condition, resulting from abnormal connections between meningeal arteries and dural sinuses. Parkinsonism with or without dementia has been reported as a presenting manifestation of DAVF. This case study aims to increase awareness of DAVF as one of the causes of rapidly progressive cognitive dysfunction and parkinsonism.
Methods: 74-year-old man developed progressive parkinsonism with impaired cognition over ten months. Systematic workup for evaluation of rapidly progressive dementia included prion disease, neurodegenerative, autoimmune, infectious, toxic-metabolic and neoplastic disorders.
Results: Brain MRI revealed T2 weighted image hyperintensities involving bilateral deep and subcortical white mater (Figure A). Moreover, some of these areas disclosed discrete hyperintensity on DWI corresponding to low values on ADC maps, reflecting cytotoxic edema secondary to ischemic injury (Figure B, C). In addition, the right transverse/sigmoid sinus was markedly dilated as were the superficial veins of both cerebral and cerebellar hemispheres (Figure D, E). CT angiography of supra-aortic trunk and cerebral arteries disclosed abnormally enlarged and tortuous vessels in the subaracnoid space, corresponding to dilated cortical vein and abnormal right dural transverse/sigmoid venous sinuses including arterializations of contrast phase in the affected sinuses due to arteriovenous shunting (Figure F). Cerebral angiogram was not performed due to poor outcome. Unfortunately, the patient died soon of SARS-CoV2.



Conclusion: DAVF is important for the differential diagnosis in patients with progressive dementia and parkinsonism. A high degree of clinical suspicion, detailed clinical examination and appropriate neuroimaging studies are crucial for early diagnosis of this disorder.
Disclosure: The authors declare that they have no competing interest. This research did not receive any specific grant from funding agencies in the public, commercial or non-profit sectors.

EPO-682

Nutrients in the Prevention of Alzheimer's Disease

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Background and aims: Alzheimer's disease (AD) is a disease caused by the complex interaction of multiple mechanisms. Epidemiologic data suggests that nutritional intake may influence it development and progression. Our aim was to assess dietary patterns and vitamins levels in people with AD as compared to healthy controls.
Methods: A cross-sectional case-control study was conducted in the Department of Neurology at the university hospital Sahloul-Sousse-Tunisia. We included volunteered patients followed for AD diagnosed in accordance to the NINCDS-ADRDA criteria and 313 healthy controls. Subjects underwent structured clinical neurological evaluation, cognitive tests, biological assessments and brain imaging. Dietary patterns were collected with a food-frequency questionnaire.
Results: 137 patients and 313 healthy controls were included. The mean age at onset was 71±9.7 years. The sex ratio of AD patients was 1.07 and 1.04 in healthy controls. The median MMSE was 14±6. High blood pressure, diabetes and high cholesterol were more frequently found in AD patients with a statistically significant difference ($p<0.001$). Consumption of spices (OR=0.33), curcuma (OR=0.15), Dry fruits (OR=0.4), fig (OR=0.24), olive oil (OR=0.25), blue fish (OR=0.31), seafood (OR=0.25) and dark chocolate (OR=0.29) was lower in patients compared to controls with a statistically significant difference. Hypocalcemia, Vitamin B12 and Vitamin D Deficiencies were significantly more frequently associated with AD.
Conclusion: Our study may provide a useful basis of existence of dietary specific patterns for AD in Tunisians. More research is needed before any of these factors can be considered a proven strategy to prevent Alzheimer's disease.
Disclosure: Nothing to disclose.

EPO-683

A case of CREUTZFELDT-JAKOB disease with atypical presentation

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Background and aims: CREUTZFELDT-JAKOB disease (CJD) is a rare neurodegenerative human spongiform encephalopathy. The sporadic form of CJD is the most common.
Methods: A 50-year-old man with unremarkable family history was hospitalized for rapidly worsening gait disturbance. He had a 12-months- history of depression and paranoid delusion. On admission, he has isolated cerebellar ataxia. MMS score was 25/30; Frontal Assessment Battery score was 16/18. Brain MRI did not reveal signs suggestive of spongiform encephalopathy. First Electroencephalogram (EEG) tracing was normal. He developed then a rapidly worsening cognitive decline, bilateral bradykinesia and rigidity, vertical gaze palsy, dysarthria and myoclonus. Psychotic symptoms have worsened with severe nocturnal hallucinations, zoopsia and agressivity. EEG was repeated and revealed periodic sharp-wave complexes. 14-3-3 protein level was elevated in the cerbrospinal fluid. The patient died 17 months after the disease onset.
Results: In our patient, clinical and paraclinical characteristics have been mostly atypical of CJD. Age of onset is early with a slow progression. Main symptoms at onset were psychiatric signs. Typical signs such as myoclonus were seen after 15-month course, which is extremely unusual in CJD.
Conclusion: Even in the absence of classical symptoms, CJD has to be considered as a differential diagnosis in rapidly progressive dementia, ataxia and parkinsonism.
Disclosure: There is no conflict of ineterest.

EPO-684

Challenges of palliative care (pc) implementation in frontotemporal dementia (ftd): a literature review

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[2] *Athens, Greece*

Background and aims: Although many articles about PC and Advance Care Planning (ACP) generally in dementia have recently been published, the implementation of PC in FTD has been limited and the special features, needs and barriers of PC in FTD remain yet to be clarified.
Methods: A comprehensive search of the literature was conducted using specified search terms (table 1). 21 articles were finally included in the study.

Databases		• PubMed • Google Scholar
Search Terms		Frontotemporal Dementia OR Dementia AND Palliative Care OR Advance Directives/Advance Care Planning OR Care Needs
Inclusion Criteria	Dementia cause	FTD
	Language	English
	Date of Publication	2000-2021
	Article Type	• Research articles • Reviews • Consensus Statements • Recommendations Papers
Number of Articles	initially identified	593
	finally included	21

Methods (further analysis)

Results: FTD showed the highest mortality risk and the most rapidly declined trajectory among the most common neurodegenerative causes of dementia. FTD patients were found to be significantly more impaired in functionality and have more radical alterations in comportment, personal relationships, religious or political values than those with Alzheimer's disease (AD) at baseline. Mild FTD patients perform normally at standard cognitive test and yet develop severe deficits in judgment and decision-making. Among the FTD spectrum, bvFTD patients showed faster cognitive and functional decline over a three-year period. In advanced stages patients suffer from autonomic dysfunction, hypertonia, mutism and compulsiveness more than AD patients. Caregivers of FTD patients are less satisfied with the provision of diagnosis, counseling, ACP and dignity preservation compared with caregivers of AD patients. To date there are no published specific guidelines or recommendations for PC or ACP in FTD.
Conclusion: High mortality, rapid trajectory, multidomain symptomatology, changes of behavior and personal values, lack of specific guidelines complicate the implementation of PC and ACP in FTD. Further research in the field is required as everyday FTD patients unmet needs are of great importancy.
Disclosure: Nothing to disclose.

EPO-685

Epidemiologic profile of patients with COVID-19 affected by ischemic stroke

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Salvador, BA, Brazil

Background and aims: Ischemic stroke is a severe complication of coronavirus disease 2019 (COVID-19) infection. Although the underlying mechanism remains uncertain, reports suggest that state of hypercoagulation, endothelial injury and inflammatory response in COVID-19 could contribute to developing ischemic stroke.
Methods: We conducted a literature review using descriptors from the MeSH portal. The search for papers was made on the PubMed platform, using the formula: ((Coronavirus Infection) OR (COVID-19)) AND (Ischemic Stroke). Only case reports and case series published from 2020 to 2021 were considered. Studies which did not meet the criteria were excluded after analysis of title and abstract. Data regarding sex, age, comorbidities, and clinical outcome of patients were collected from the eligible articles.
Results: The search strategy resulted in 65 studies, of which 39 were included. After reading, nine were excluded and a total of 61 patients were evaluated, of those, 57 patients with a proper ischemic stroke diagnosis were considered for this paper. There were 16 female and 46 male patients, the median age was 61.2 years old, the most common comorbidities were high blood pressure (23 patients), diabetes mellitus (18 patients) and tobacco exposure (7 patients).
Conclusion: From that, it is possible to conclude that the epidemiologic profile for COVID-19 related ischemic stroke is a male patient in the seventh decade of life, with high blood pressure and diabetes mellitus. The most likely clinical outcome is recovery with disability.
Disclosure: Nothing to disclose.

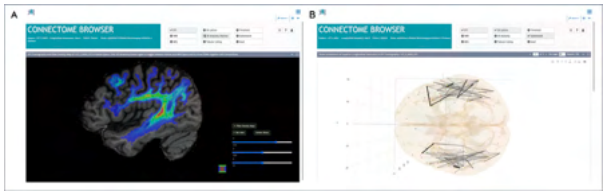
EPO-686

Opposing patterns of brain rewiring in Alzheimer's disease patients at early vs late stages

Y. Li, M. Butz-Ostendorf
Brain Science, Biomax Informatics AG, Planegg, Germany

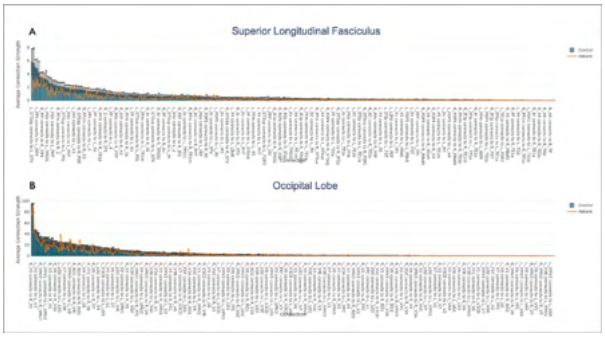
Background and aims: Grey matter loss especially in hippocampal areas of Alzheimer's disease (AD) brains is well known and occurs from early stages on while visual areas are less affected. While the spatio-temporal pattern of GM loss is quite well understood, the course of white matter (WM) loss in response to GM degeneration remains contradictory. Therefore, we re-assessed WM densities at and changes between two measurements in 25 randomly chosen AD patients from the ADNI3 cohort [1] and compared them to 27 matched controls.

Methods: We computed full brain probabilistic tractography from probabilistic fiber tracking by MrTrix3 [2]. ROI to ROI connectivity (HCP MMP 1.0 brain atlas) was compared between Superior Longitudinal Fasciculus (SLF) and occipital cortex in two longitudinal DTI scans with one year interval by the help of NICARA (www.nicara.eu) [3].

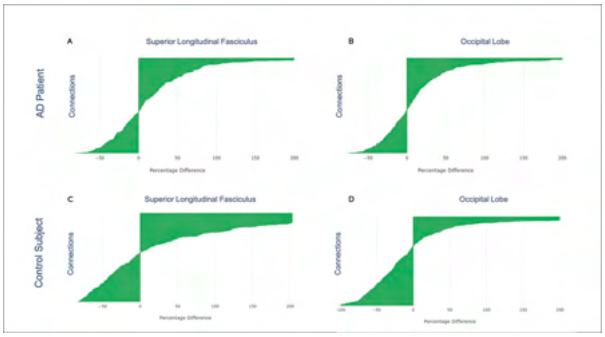


Superior Longitudinal Fasciculus in an AD patient from ADNI3. A. Fiber Density Map from probabilistic fiber tracking considering streamlines connecting ROIs of SLF. B. 3D lattice graph of SLF in NICARA (nicara.eu) used for quantitative comparisons.

Results: Surprisingly, AD patients showed two opposing patterns of brain connectivity and rewiring [4]. The first pattern was characterized by pronounced changes in connectivity associated with a hyperconnectivity in the SLF but less so in occipital cortex. The second pattern showed reduced rewiring with a reduced SLF connectivity. The observations did not correlate with age, nor with disease onset but were associated with decreasing MMSE scores.



WM connection strengths measured in A. the SLF and B. the occipital cortex of one patient compared to age-matched controls. This patient's connection strengths are representative for the first pattern of reduced connectivity and rewiring.



Percentage changes in connection strengths (x-axis) of A. SLF and B. occipital cortex connections (y-axis) in the same patient and C. and D. in control subject.

Conclusion: This study is the first that reports a reduced brain rewiring in AD patients. Opposing patterns of brain rewiring could be an expression of different stages of WM reorganization in AD. Our findings point to the urgent need for including longitudinal DTI tractographies in routine brain scans and clinical trials.

Disclosure: The authors JL and MBO are employed with Biomax Informatics AG and will therefore be affected by any commercial implications caused by this scientific contribution.

EPO-687

Grip Strength Response to Changes in Serum IG Trough Level in Patients with Multifocal Motor Neuropathy on IVIG

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[1] Cambridge, United States, [2] Austria

Background and aims: IV IG (IVIG) is an effective treatment for multifocal motor neuropathy (MMN). We examined how grip strength (GS) responded to serum immunoglobulin G (IgG) trough (IgG[trough]) alterations in MMN.
Methods: In this post hoc analysis of an IVIG, 10% phase three trial (NCT00666263), adults with MMN on stable IVIG therapy were randomised (1:1) to two sequences of five 12-week treatment periods (S1 [n=22]: IVIG-IVIG-IVIG-placebo-IVIG; S2 [n=22]: IVIG-placebo-IVIG-IVIG-IVIG). Periods 1, 3, and 5 were open-label IVIG; periods two and four were double blinded. IgG(trough) and GS were measured at the beginning and end of each period, respectively. An ANOVA compared GS during IVIG vs placebo. The association between IgG(trough) and GS was evaluated by linear regression.
Results: In patients (12 women/32 men; mean±SD age: 51.6±10.3 y) switching from IVIG to placebo, GS rapidly declined in the more affected hand (mean±SD change: 28.7±25.7% for S1; 27.1±41.1% for S2). Least square means of percent change in GS in the more affected hand differed significantly between IVIG and placebo (35.13%; p=0.005). At the individual level, in most patients, directional changes in IgG(trough) and GS were similar. Percent change of GS vs IgG(trough) or percent change of IgG(trough) showed no correlation at the group level. Findings were similar for the less affected hand.
Conclusion: GS response to serum IgG level alterations was patient specific. Results highlight the importance of maintaining stable IgG levels on an individual basis in MMN.
Disclosure: Shire US Inc., a Takeda company, funded this study. Baxalta US Inc., a Takeda company, funded medical writing support.

EPO-688

Neurology and Psychiatry: a challenging border for diagnosis

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Background and aims: Rapidly progressive neurodegenerative conditions represent an uncommon cause of disease. After discarding the most frequent etiologies, diagnosis can be challenging and sometimes unachievable, especially when psychiatric comorbidities appear.
Methods: A 69-year-old woman with history of hypertension and diabetes presents with two-month gait instability and depression. Exam showed mild axial rigidity, bradykinesia and broad-based gait. Over the next months symptoms fluctuated but progressed adding hypomimia, dysarthria, dysphagia requiring a nasogastric tube for feeding, leading her to be bedridden in a catatonic-like state.
Results: Infections, autoimmunity and malignancy were ruled out. Three cerebral MRIs, a cervical MRI, an I-123 DaTscan-SPECT, an FDG-PET scan, two EEG and two lumbar punctures (RT-QuIC, oligoclonal bands, onconeuronal and neuronal surface antibodies) were performed. The only findings where subtle frontal hypometabolism on FDG-PET scan, anti-GAD antibodies on serum and CSF, elevated total tau protein and minimal B-amyloid decrease on CSF. Psychiatry discarded a psychiatric origin several times. She was treated with levodopa and antidepressants without improvement, three cycles of intravenous immunoglobulins (IVIg) with only a subtle improvement with the first one, and a cycle of high dose of methylprednisolone without response. After nine months, the patient passed away from bronchoaspiration. Autopsy wasn't performed due to family reasons.
Conclusion: We showcase a complex case without a definitive diagnosis. An exhaustive study was performed, with inconclusive results for any etiology. The rapid progression and the non-response to treatments, along with the psychiatric symptoms, hindered the diagnostic process. Cases like this should encourage to perform autopsies to increase our knowledge.
Disclosure: Nothing to disclose.

EPO-689

Carotid-cavernous fistula as a rare complication of radiofrequency ablation for MS-related trigeminal neuralgia

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Background and aims: Trigeminal neuralgia (TN) related to Multiple Sclerosis (MS) lesions is a challenging condition. We report a rare complication of radiofrequency ablation (RA) for medically-refractory TN.
Methods: N/A.
Results: A 39-year-old man with relapsing-remitting MS since 1998 presented with refractory right TN in 2016. After trials of medical therapy with no adequate pain control, he was treated with Gamma-knife radiosurgery in 2017, but recurrence of symptoms led to RA in the following year. After an initial period of pain relief that lasted for nine months, a second RA was performed in December of 2019, with no immediate complications. In the following two months, he reported an insidious onset of ocular discomfort and red eye on the right side. Upon examination, he presented with proptosis, ocular bruit and chemosis of the right eye. Ophthalmological assessment disclosed increased intraocular pressure and arterialization of the conjunctival and episcleral vessels on the right side. Brain CT and CT angiography confirmed the presence of a right direct carotid-cavernous fistula (CCF). Endovascular treatment via the internal carotid artery with a transarterial approach was successful, and ocular symptoms resolved within days.
Conclusion: CCF is a rare complication of RA for TN (estimated to be 0.06%), and it is usually associated with improper needle penetration of the foramen ovale. Given the fact that patients with MS-related TN are much less likely to attain long-term pain relief with a single invasive treatment, complications such as iatrogenic CCF should be taken into account during the pursuit of a greater pain relief.
Disclosure: Nothing to disclose.

EPO-690

A first case of primary diffuse leptomeningeal melanomatosis in Belarusian child: our observation

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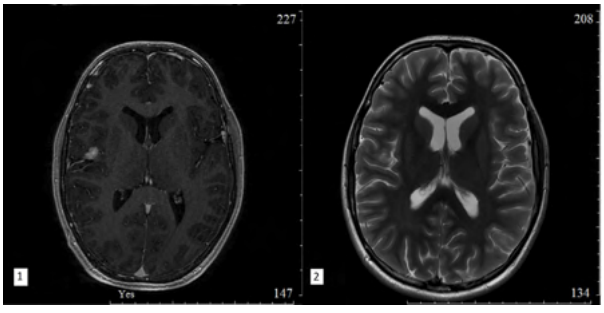
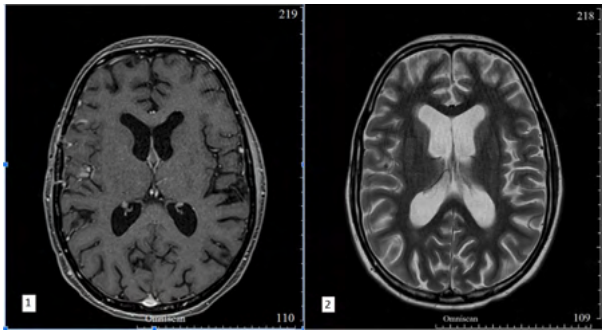
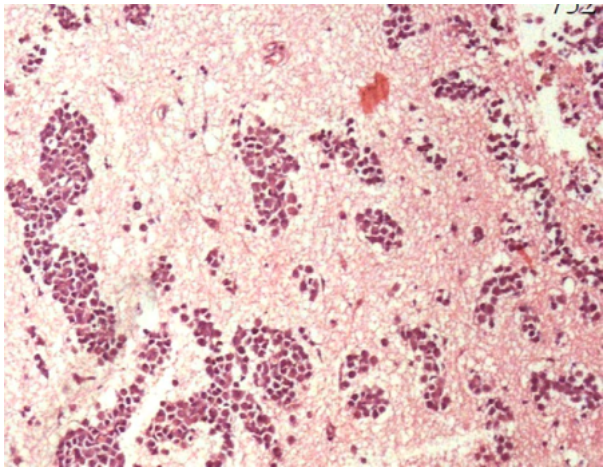
Background and aims: Primary diffuse leptomeningeal melanomatosis (PDLM) is a rare type of primary brain tumor (0.05–0.17%), especially in children. Due to high aggressiveness patients have a poor prognosis.
Methods: Description of our case of observation of a child patient with PDLM. It is the first pediatric case for our Center from 1997 to the present.
Results: A 12-year-old boy became ill when he developed hemiparesis and numbness in his left limbs within an hour. MRI of the brain showed lesions of the right precentral gyrus with damage to the meninges. The patient had frequent sensory seizures with a motor component in his left limbs, which is why VPA was prescribed. 10 days after the onset of the disease, a partial resection of the tumor was performed under the control of neuronavigation. According to the histological examination, the absence of BRAF mutations, MRI data and the presence of atypical cells in the CSF, absence of skin and internal organs damage – was diagnosed PDLM. The patient received radiation therapy (36 Gr) with IT MTX, as well as of eight IV Pembrolizumab. Control MRIs do not reveal progression. After seven months the patient retains mild left-sided hemiparesis. Due to the persistence of seizures, LEV was added.



MRI axial scans 1) T1+contrast and 2) T2 before treatment



MRI axial scans 1) T1+contrast and 2) T2 before treatment



Staining with hematoxylin and eosin. Many large polymorphic cells with large nuclei and coarse chromatin.

Conclusion: PDLM-is a rare tumor, especially in childhood. With radiological signs of a brain tumor, neurosurgery can allow you to make the correct diagnosis and start treatment at an earlier time. The use of radiation therapy in combination with MTX and Pembolizumab may be effective in the treatment of PDLM.
Disclosure: Nothing to disclose.

EPO-691

Double trouble: can Guillain-Barré syndrome and botulism coexist?

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Background and aims: The differential diagnosis of acute flaccid paralysis with cranial nerve involvement is extensive and Guillain Barre Syndrome(GBS) is one of the most common etiologies. GBS is, however, rare in infants under six months old.
Methods: .
Results: Our patient is a three-month-old infant that presented with irritability, bilateral ptosis, and oculomotor disturbance developing over 24 h. Neurological examination revealed sluggish pupillary responses, complex ophthalmoparesis,and bilateral ptosis. Over 24-hours he developed bilateral facial palsy, bulbar dysfunction, areflexic flaccid tetraparesis,and paroxysmal tachycardia with hypertension. He required mechanical ventilation and admission to ICU. Initial investigation revealed albuminocitological dissociation and MRI with diffuse Gd+ root uptake. GBS was assumed and he was treated with IvIG(2g/kg). Nerve conduction studies were suggestive of demyelinating sensory-motor polyneuropathy, and antigangliosides were positive for IgM anti-GM2. On the 16th day after admission, we received a positive result for fecal botulinum toxin type B, which was not confirmed on further trials or in household foodstuff (he was fed with formula). Despite clinical improvement, he maintained ophthalmoparesis and inconsistent visual response. A second MRI revealed active hydrocephalus, requiring ventricular-peritoneal shunting. Currently, at 15 months of age, he walks unaided and has regained osteotendinous reflexes. Both nerve conduction studies and antiganglioside antibodies normalized six months after initial presentation.
Conclusion: The hypothesis of infantile botulism in a descending tetraparesis was considered, but did not explain the complete clinical picture. We therefore believe this was the first case described of a Guillain-barré syndrome at an age younger than six months, complicated by hydrocephalus.
Disclosure: Nothing to disclose.

EPO-692

Frontotemporal dementia-motor neuron disease continuum: a different phenotype

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Background and aims: Frontotemporal dementia (FTD) and motor neuron disease (MND) are considered a continuum with genetic and neuropathological overlap. Cognitive profile is most often compatible with behavioral variant of FTD and amyotrophic lateral sclerosis corresponds to the commonest pattern of MND.
Methods: Case report of FTD-MND.
Results: A 57-year-old woman, nurse, right-handed, presented with an eight months history of speech and memory issues. She spoke slowly, had wordfinding and naming difficulties. Comprehension, reading and writing were preserved. Neurological examination revealed Mini-Mental State Examination of 27/30, slow, telegraphic and hesitant speech, short sentences, anomia, syllable suppression or extension and hyperreflexia on upper right limb. Neuropsychological assessment disclosed progressive apraxia of speech dominant over non-fluent language disorder. Brain MRI demonstrated asymmetrical temporal lobe atrophy (left>right). FDG-PET showed hypometabolism in the left parietal-temporal and frontal lobes. Over the next two years her state rapidly deteriorated with pseudobulbar affect, anarthria, inability to protrude the tongue, dysphagia, asymetric hyperreflexive spastic tetraparesia (right>left), bilateral Tromner-Hoffmann and Babinski signs, without wasting or fasciculations. Cervical MRI excluded spinal cord compression and electromyography was unremarkable. C9orf72 gene was normal and genetic testing for FTD-MND was requested. Currently she is in a wheelchair and totally dependent on daily living activities; comprehension and writing remain preserved.
Conclusion: Progressive speech impairment is a common presenting complaint heralding neurodegenerative disease. In our case, an isolated speech disturbance associated with upper motor signs suggests a disease in the FTD-MND spectrum, with primary lateral sclerosis phenotype what is exceptional. Genetic testing will be crucial to disclose the etiology.
Disclosure: Nothing to disclose.

EPO-693

A case of Morvan's syndrome with non-characterized neuronal surface antibodies

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Background and aims: Morvan syndrome is recognized as a constellation of neuromyotonia, dysautonomia and encephalopathy with marked insomnia, classically associated with CASPR2 and LGI1-antibodies.
Methods: We describe a patient with Morvan spectrum symptoms and a novel neuronal-surface reactivity.
Results: A 68-year-old man consulted for subacute anxiety, nocturnal hyperhidrosis, severe insomnia and intermittent diarrhea over three months. He had a history of anti-RACh+ generalized myasthenia without thymoma, stable under low-dose immunotherapy. On examination, no cognitive, cranial nerve, muscle strength, coordination or sensory deficits or fatigability were detected. Multifocal fasciculations in facial, forearms and leg muscles, and mild choreiform movements were observed. Needle electromyography (Fig1) showed peripheral nerve hyperexcitability signs. Polysomnography evidenced low sleep efficiency and REM sleep behavior disorder, with difficulty in initiating and consolidating sleep confirmed by actimetry (Fig2). Serum and CSF studies detected CRMP5-antibodies, and neuronal surface immunoreactivity on brain immunohistochemistry (Fig3). All currently known neuronal autoantibodies were negative. A body PET scan and thoracic MRI showed a mildly hypermetabolic anterior mediastinal mass consistent with thymoma that was surgically resected. He was further treated with steroids and IVIG with good response. One month later, he was brought to the emergency room for syncope. He had severe dyspnea and dysautonomia (hyperhidrosis, tachycardia, tachypnea, hypertension) that required non-invasive mechanical ventilation and treatment with clonidine and propranolol in the ICU. He further received six courses of plasma exchange and rituximab, resulting in progressive improvement.

Fig 1. Needle electromyography showing *doublets*.

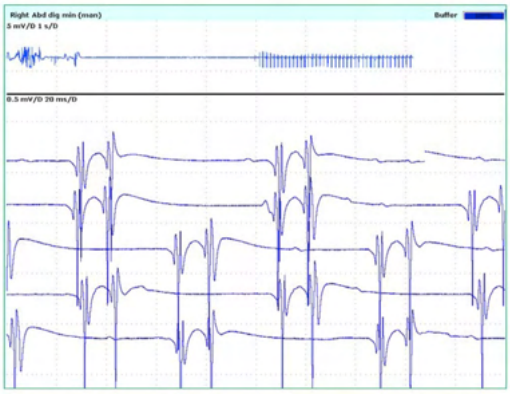


Fig 2. The actimetry studies showed motor activity of the patient during all day without proper rest.

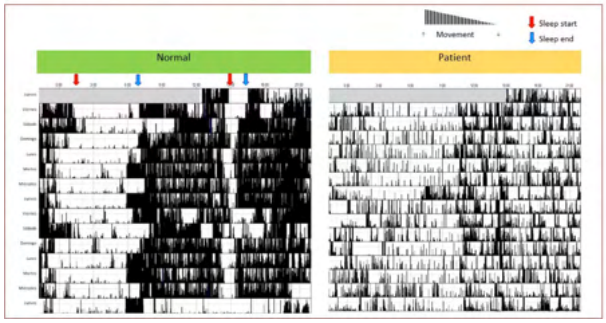
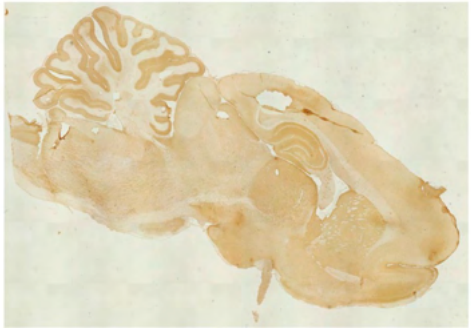


Fig 3. Immunohistochemistry on rat brain section showing the presence of neuronal surface immunoreactivity against unknown antigen.



Conclusion: Thymomas frequently associate with multiple neurological syndromes and the presence of several coexisting autoantibodies.
Disclosure: No disclosures.

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EPO-694

Convexity Subarachnoid Haemorrhage and Arterial Occlusion or Stenosis: a Retrospective study

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Background and aims: Acute nontraumatic convexity subarachnoid haemorrhage (cSAH) is a rare entity, caused by a wide spectrum of vascular and non-vascular pathology. While cSAH most frequently follows from rupture of vascular malformations, venous thrombosis or amyloid angiopathy, it may also be associated with atherosclerostic disease, through mechanisms not yet known.
Methods: Aims: Characterisation of clinical presentation, imaging findings and prognosis of patients with nontraumatic cSAH associated with arterial occlusion/stenosis. **Methods:** Selection of patients admitted to the Neurology department with nontraumatic cSAH and arterial occlusion/stenosis, between January 2012 and August 2020. Review of clinical charts.
Results: Nine patients with nontraumatic nonaneurysmal cSAH were identified, of whom six presented arterial stenosis/occlusion and acute ischaemic stroke (mean age: 60 y.o.). Headache was present in two patients. Carotid artery occlusion was documented in three patients (2 of which also had contralateral internal carotid artery stenosis over 70%), carotid near-occlusion in two patients, and MCA M1 segment occlusion in another patient. cSAH was ipsilateral to the identified ischaemic lesion in all patients, however there was no clearly identifiable pattern in the relationship between cSAH location and arterial stenosis/occlusion. Four patients underwent revascularization therapy. Five patients had modified Rankin Scale score at discharge of one. No cases of rebleeding were documented.
Conclusion: In our series the relation of cSAH with ischaemic lesion (rather than arterial occlusion/stenosis) suggests that cSAH results from an acute haemodynamic insult, leading to congestion and rupture of leptomeningeal collateral vessels. Despite varying clinical courses, all patients had a good prognosis and there were no cases of rebleeding.
Disclosure: No disclosures.

EPO-695

Point of Care Testing of Direct Oral Anticoagulants in Patients with Stroke at the Emergency

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Background and aims: The incidence of the stroke is increasing and its adequate treatment is still challenging. One of the key factors in management of stroke patients is the coagulation status, which can be significantly affected in patients on direct oral anticoagulants (DOACs).
Methods: Management of stroke requires fast assessment of coagulation status, however patient´s history is often unknown and standard coagulation laboratory tests are time consuming. Therefore, rapid identification of patients on DOACs is important and the Dipstick® point of care test (POCT) is available for this purpose. It is a diagnostic urine strip test, intended for qualitative detection of DOACs (Dabigatran, Apixaban, Edoxaban and Rivaroxaban). The result can be read with naked eye by or by using a photometric reader (DOASENSE Reader®). Dipstick® POCT was performed since 15th May 2002 in all stroke patients with unknown medical history who were admitted to Emergency department of University hospital Brno, Brno, Czech Republic.
Results: Between 15 May 2020 and 31 December 2020 193 stroke patients were admitted at the Emergency department. Dipstick® POCT was performed in 23 patients and the test was positive in eight cases (35%).
Conclusion: We were able to quickly detect an effective level of DOAC in the blood in eight patients with unknown medical history. This information significantly influenced the therapeutic process.
Disclosure: The authors declare that they have no conflict of interest.

EPO-696

Demographic and clinical characteristic of patients disqualified from mechanical thrombectomy: single-center experience

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Background and aims: Mechanical thrombectomy (MT) is a treatment of choice for acute ischemic stroke (AIS) due to large vessel occlusion (LVO). However, there is a proportion of patients who reach the selection procedure at the Comprehensive Stroke Center (CSC), but do not fulfill criteria for MT. The study was aimed to characterize AIS patients who enter the selection procedure for MT, but finally were disqualified from this procedure.
Methods: The study was performed in the CSC in Krakow (2019-2020), which serves MT for a population of 3.36 million. Several demographic and clinical parameters were analyzed, including standardized time-points evaluated in AIS, radiological parameters (Rapid software), the reasons for disqualification from MT and outcome on discharge measured by the mRS.
Results: 478 patients were included (50% females; mean age: 69 years). MT was performed in 314 patients (65.7%) and 164 patients were disqualified (34.3%). Disqualified patients had significantly longer time-lapses between the standardized time-points evaluated in AIS ($p<0.05$), and had worse outcome on discharge ($p<0.05$). The reasons for disqualification were: brain infarction on CT (58.9%); effective recanalization after rt-PAIV (24.0%); spontaneous recanalization (1.2%), hemorrhagic transformation on CT (3.6%); abnormal anatomy of brain vessels (5.4%); patients' refusal (1.2%); the lack of access to anesthesiologist (0.6%), others (4.8%).
Conclusion: In this cohort, one third of patients were disqualified from MT; mostly due to brain infarction on neuroimaging. They reached measured time-points much later than those who had MT. Future efforts should be addressed to speed-up the transfer of AIS patients to the CSC.
Disclosure: ERA-NET-NEURON/21/2020 iBioStroke grant.

EPO-697

The role of soluble vascular adhesion molecule-1 in the pathogenesis of cerebral small vessel disease

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Background and aims: Cerebral small vessel disease (SVD) is a leading cause of cognitive impairments and stroke.The inability to direct visualize of small vessels, justifies the search for relevant markers. Endothelial dysfunction is thought to maintain inflammation and vascular wall permeability in SVD. Soluble vascular adhesion molecule-1(sVCAM-1) expresses by activated endothelium and participate in tight adhesion, transendothelial migration of leukocytes via blood-brain barrier(BBB).
Methods: 71 patients (48f.,60.5±6.9years) with SVD and 21 volunteers (15f., 57.3±5.2) without brain pathology were included in study. Brain 3T MRI to assess MRI signs of SVD (white matter hyperintensity(WMH), lacunes, microbleeds (MBs), perivascular spaces (PVS)) and volume of WMH was performed.sVCAM-1 level was measured using ELISA.
Results: 17 patients had Fazekas (F)1 WMH,24–F2, 30–F3 stage. A statistically significant positive correlation was found between the volume of WMH and the level of sVCAM-1($R=0.301$,$p=0.034$).In the case of lacunes in the basal ganglia, the level of sVCAM-1 was higher in the group with single lacunes compared to the group without lacunes($p=0.001$), and in the case of multiple lacunes it was lower than in the group with single lacunes($p=0.001$).An increase in the level of sVCAM-1 influenced the size of PVS in the semioval center($p=0.015$).
Conclusion: The relationship between an increase in sVCAM-1 with the severity of WMH and PVS, but not with lacunes and MBs indicates its decisive role in the inflammation and BBB permeability in SVD. A decrease in sVCAM-1 in multiple lacunes may correspond to endothelial depletion at this stage and the significance of other mechanisms in the small vessel damage.
Disclosure: The authors declare no conflict of interest.

EPO-698

The effect of standardized antiplatelet therapy on the in-hospital recurrence in AIS patient

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Background and aims: Acute ischemic stroke has a high risk of recurrence. The in-hospital recurrence rate of ischemic stroke in AIS patients was 0.8%~7.08%. In 2013, the CHANCE TRAIL drew a conclusion that among patients with TIA or minor stroke, the combination of clopidogrel and aspirin is superior to aspirin alone for reducing the risk of stroke in the first 90 days. The purpose of this study was to assess the effect of standardized antiplatelet therapy on the in-hospital recurrence in AIS patients.

Methods: 1,502 patients with acute ischemic stroke were enrolled in the study. 975 patients were admitted to the hospital between 2012 and 2013, and the other 314 patients were admitted in 2016. The primary endpoint was a recurrent stroke which was defined as a new and persisting (>24 hours) neurological deficit. The onset of the new neurological deficit >24 hours after the index event. Other causes for neurological deterioration were excluded.

Results: The in-hospital recurrence rate decreased after the guideline updated (5.9% vs. 3.2%). The recurrence rate was significantly lower in LAA subtype before (2012-2013) and after (2016) the guideline updated (p=0.004). In LAA patients, we found that the proportion of DAPT use was significantly higher in 2016, especially in no-recurrence group (p<0.001).

Table 1. The in-hospital recurrence rates in different stroke subtypes before (2012-2013) and after (2016) the guideline updated.

TOAST		Total (n=1502)	2012-2013 (n=975)	2016 (n=527)	P value
LAA	NoRe (%)	691 (93.0%)	389 (90.7)	302 (96.2)	0.004
	Re (%)	52 (7.0%)	40 (9.3)	12 (3.8)	
	Total	743	429	314	
CE	NoRe (%)	114 (93.4)	74 (92.5)	40 (95.2)	0.713
	Re (%)	8 (6.6)	6 (7.5)	2 (4.8)	
	Total	122	80	42	
SV	NoRe (%)	376 (99.7)	233 (100.0)	143 (99.3)	0.382
	Re (%)	1 (0.3)	0 (0.0)	1 (0.7)	
	Total	377	233	144	
OD	NoRe (%)	21 (84.0)	17 (85.0)	4 (80.0)	1.000
	Re (%)	4 (16.0)	3 (15.0)	1 (20.0)	
	Total	25	20	5	
UD	NoRe (%)	225 (95.7)	204 (95.8)	21 (95.5)	1.000
	Re (%)	10 (4.3)	9 (4.2)	1 (10.0)	
	Total	235	213	22	

TOAST: the Trial of Org10172 in Acute Stroke Treatment; LAA: large artery atherosclerosis; CE: cardiac embolism; SV: small vessel disease; OD: other causes; UD: unknown causes; Re: recurrence; NoRe: No recurrence.

The in-hospital recurrence rates in different stroke subtypes before (2012–2013) and after (2016) the guideline updated.

Table 2. The relationship between in-hospital stroke recurrence and DAPT use in LAA patients

		2012-2013 (n=429)	2016 (n=314)	P value
No-Recurrence	NoDAPT(%)	219 (56.3)	74 (24.5)	<0.001
	DAPT(%)	170 (43.7)	228 (75.5)	
	Total	389	302	
Recurrence	NoDAPT(%)	20 (50)	3 (25)	0.188
	DAPT(%)	20 (50)	9 (75)	
	Total	40	12	

DAPT: dual antiplatelet therapy; LAA: large artery atherosclerosis.

The relationship between in-hospital stroke recurrence and DAPT use in LAA patients.

Conclusion: The use of DAPT can decrease the in-hospital recurrence in AIS patients with LAA subtype. Since patients with standardized antiplatelet therapy can also meet the risk of in-hospital recurrence, there might be other risk factors .

Disclosure: We declare no competing interests.

EPO-699

An audit of anticoagulant therapy in patients with Atrial Fibrillation within Church Street Medical Centre

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Manchester, United Kingdom

Background and aims: Patients with Atrial fibrillation (AF) have a five-fold higher risk of stroke than those without it. Approximately 15% of all strokes are caused by AF, which amounts to 12,500 strokes annually in England. NICE states that anticoagulants are the treatment of choice in AF and they should not be withheld due to risk of a fall. To improve the care of our patients, it was decided to compare our current performance in AF management with the latest NICE guidelines.
Methods: Data was collected using system one, patient records were examined retrospectively. All patients with AF and a CHA2DS2VASc score of >2 for women and >1 for men were included**Results:** The initial audit showed 233 AF patients within the practice, with 43.8% (102) not on anticoagulants. Furthermore, 78% of those 102 patients had not been offered treatment. These patients were identified, reviewed and offered treatment accordingly. A proposal was made to utilise GRASP-AF and the Warfarin Patient Safety Audit Tool annually. A second audit was conducted in 2018 to measure the impact of the proposal. The results showed a marked improvement, with only 17.9% (45) of 252 AF patients not on anticoagulation. The annual risk of stroke in the practice dropped from 3.7% in March 2016 to 2.1% in November 2018.
Conclusion: This audit identified shortcomings in the management of AF within the practice. The implementation of the annual GRASP-AF and Warfarin Patient Safety Audit tool resulted in an improvement in AF management and a subsequent reduced stroke risk within the practice.
Disclosure: No conflicts of interest.

EPO-700

Serum biomarkers of ischemic stroke

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Background and aims: In this study we evaluated serum levels of cerebral ischemia biomarkers such as neuron-specific enolase (NSE), glial fibrillar acid protein (GFAP) and NR2-antibodies for NMDA receptor (NR2) in acute period of ischemic stroke (IS).
Methods: 40 patients were diagnosed with IS clinically and with neuroimaging. Blood samples were taken at 72 hours (point 1, p1) and after 10–14 days (point 2, p2) since IS onset, serum biomarker levels evaluated with ELISA kit. Patients were evaluated clinically using NIHSS, Barthel, Rivermead and modified Rankin (mRS) scales at p1 and p2.
Results: In most cases we observed elevated levels of NSE and GFAP at p1, lowering at p2 (p=0,007, 0,22), reaching reference values (RV) in 29% of patients for NSE and in 92.5% for GFAP, while NR2 levels were within RV at p1 and rising at p2 (p=0,007). In patients with higher initial NIHSS score p1-levels of NSE and GFAP were higher (p=0,008, 0,058), lowering altogether (p=0,016, 0,893) and NR2 was lower (p=0,047), rising significally with NIHSS scores (p=0,041). Higher levels of NSE and NR2 at both p1 and p2 (p=0,012, 0,014 and p=0,0001, 0,00001) and of GFAP at p1 (p=0,0001) were found in cases with higher mRS scores, and for such patients NR2 levels were rising while lowering for others (p=0,06). Correlations were discovered between higher NIHSS initial and lower discharge Barthel scores and higher NSE and GFAP p1-levels.
Conclusion: The links between serum biomarker levels and the degree of neurological deficit and functional outcomes in acute IS period prove their diagnostic and prognostic value.
Disclosure: Nothing to disclose.

EPO-701

Correlation of S-100B protein serum level with radiological measures of infarct volume in ischemic stroke

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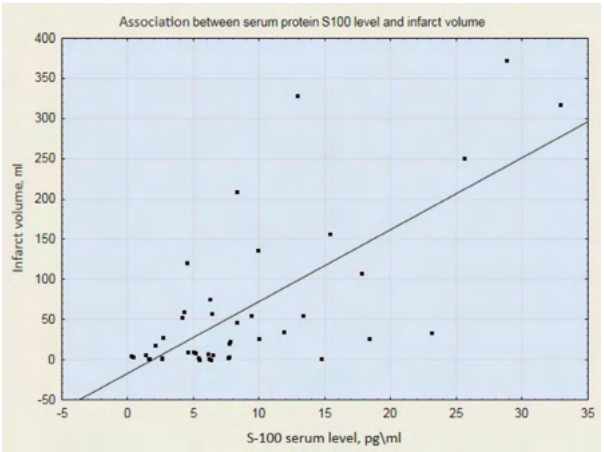
Background and aims: Better techniques are needed to monitor infarction volume and predict neurological outcome after ischemic brain infarction. Astroglial protein S100B is elevated in peripheral blood in the first days after acute ischemic stroke. **Aim:** to evaluate the effectiveness of measurement S-100B protein serum level in blood samples from patients with acute ischemic stroke for assessing infarct size.

Methods: The study was carried out in a total 45 patients with acute ischemic stroke in the middle cerebral artery (middle age 73±6.1 years). Control group includes 40 healthy individuals (middle age 70±3.4 years). Infarct volume was measured by volumetric CT or MRI on the second day from the stroke onset. Blood sampling were performed on the second day from the stroke onset. Serum S-100B level was determined by using DY1820-05 Human S100B DuoSet ELISA-kit (R&D Systems, USA).

Results: Serum S-100B concentration was significantly elevated in patients with acute ischemic stroke 6,4 (4,5; 12,9) pg/ml compared to controls 2,6 (1,8; 5,8) pg/ml (Mann-Whitney U test, p<0.001). S-100B protein level significantly correlated with infarct volume on the second day from the stroke onset (Spearman rank correlation test r=0,551; p<0,05).



Conclusion: Higher S100B values indicated significantly larger infarction volumes. The present study suggests measurement of serum S-100B protein could be a useful prognostic marker of the infarct volume in patients with acute ischemic stroke.

Disclosure: Nothing to disclose.

EPO-702

Relationships between serum Brain-derived neurotrophic factor levels and infarct volumes in acute ischemic stroke

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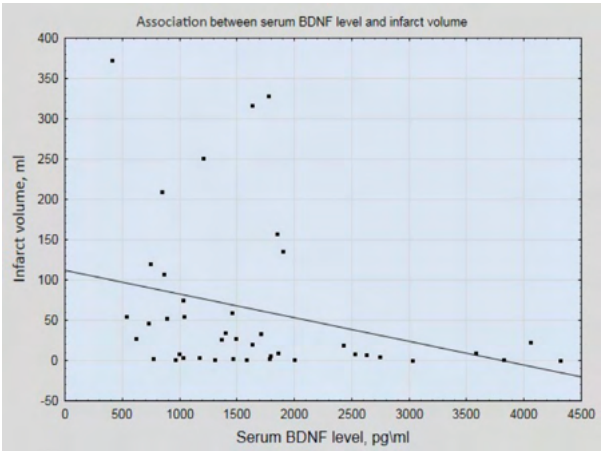
Background and aims: Brain-derived neurotrophic factor (BDNF) has a central role in brain plasticity by mediating changes in cortical thickness and synaptic density. BDNF also possesses other neuroprotective effects including anti-apoptosis, anti-oxidation, and suppression of autophagy. **Aim:** to investigate the association between infarct volume and BDNF on the second day from the stroke onset in patients with acute ischemic stroke.

Methods: The study was carried out in a total 45 patients with acute ischemic stroke in the middle cerebral artery (middle age 73±6.1 years). Control group includes 40 healthy individuals (middle age 70±3.4 years). Infarct volume was measured by volumetric CT or MRI on the second day from the stroke onset. Blood sampling were performed on the second day from the stroke onset. Serum BDNF was determined by MAGPIX multiplex analyzer (Luminex, USA) using xMAP® Technology.

Results: Serum BDNF level was lower in patients with ischemic stroke 1,459 (960; 1,859) pg/ml than in the control group 3,959 (2,208; 5,251) pg/ml (Mann-Whitney U test p< 0,001). Serum BDNF level has significant negative correlation with infarct volume on the second day from the the stroke onset (Spearman rank correlation test r=-0,454; p<0,05).



Conclusion: Larger stroke infarct volumes are associated with lower levels of BDNF on the second day from the stroke onset. Further investigations are suggested to elucidate the role of BDNF as part of a potential neuroprotective strategy.

Disclosure: Nothing to disclose.

EPO-703

Management and outcomes of recombinant tissue plasminogen activator associated bleeding in acute ischemic stroke

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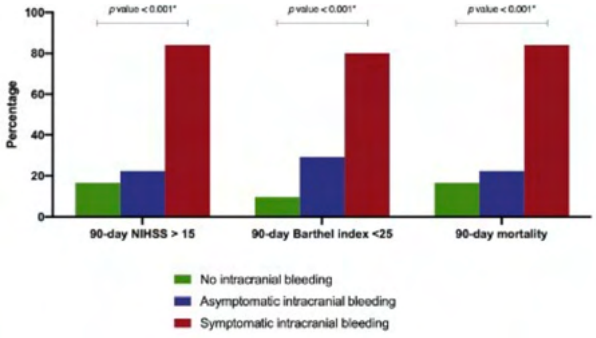
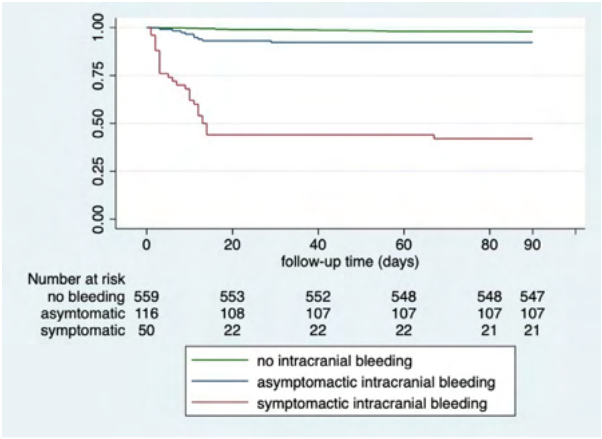
Background and aims: Intracranial hemorrhage (ICH) is the most devastating complication of recombinant tissue plasminogen activator (rt-PA) treatment in acute ischemic stroke patients. Data on management and outcomes rt-PA associated ICH are limited.
Methods: We conducted an analysis of the data derived from the Maharaj Nakorn Chiang Mai Hospital Stroke registry between 1995 and 2019. We included consecutive ischemic stroke patients who were 18 or older and received rt-PA. Study outcomes were incidence and characteristic of ICH, ICH management, 90-day National Institute of Health Stroke Scale (NIHSS), Barthel index and all-cause mortality.
Results: Of 725 rt-PA treated patient, 50 (6.9%, 95% confidence interval (CI) 5.2-9.0) had symptomatic ICH (sICH) and 166 (16.0%, 95% CI 13.4–18.9) had asymptomatic ICH (aICH). Cardioembolic stroke, prior-antiplatelet use, NIHSS >15, and Barthel index <25 at stroke diagnosis were risk factors of ICH. Patients with sICH had more parenchymal hemorrhage (98.0% vs. 18.1%, p<0.001) comparing to aICH. Fresh Frozen Plasma and cryoprecipitate were the most common product used to reverse anticoagulant effect. Craniotomy was performed in 60% and 1% of cICH and aICH patients. At 90 days, patients who had sICH had poorer clinical outcomes (NIHSS, Barthel index and death) as compared to aICH and those without ICH. Compared to non-ICH patients, sICH and aICH were associated with increased risk of 90-day mortality, Hazard ratio (HR), 95% CI was 40.6, 19.5–84.5 and 4.5, 1.9–10.3, respectively.



A 90-day NIHSS, Barthel index and mortality in patients receiving rt-PA.



The Kaplan-Meier curve of overall survival in patients receiving rt-PA.

Conclusion: rt-PA associated ICH increased risk of morbidity and mortality outcomes, regardless of symptom. Further clinical trials focusing on treatment of rt-PA associated ICH is urgently needed.
Disclosure: Nothing to disclose.

EPO-704

Ischemic stroke after SARS-CoV-2 associated pneumonia in a 16-year-old: A case report

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Background and aims: SARS-CoV-2 infection results in severe acute respiratory syndrome with a varied number of systemic complications. Elevated pro-inflammatory cytokines (IL-2,6,7, TNF-), inflammatory markers and changes in the state of coagulation with elevated levels of d-Dimer and fibrinogen, increase the risk of thromboembolic events such as ischemic stroke, deep vein thrombosis (DVT) , pulmonary thromboembolism (PTE) and others.
Methods: A 16-year-old female presented with complaints of acute headache, fever, dry cough and lethargy. She was hospitalized with laboratory confirmed tests for SARS-CoV-2 and due to an onset of acute respiratory distress, underwent mechanical ventilation. Physical and neurological examinations (NE), Chest X-rays, Brain and lung Computed tomography (CT) with angiography, Echocardiography (EchoCG), Abdominal ultrasound, tests for Thrombophilia, ANA, ANCA screening and dry blood test for Fabry disease were performed.
Results: NE revealed a right-sided central facial nerve lesion with hemiparesis more pronounced in the upper limb. Brain CT showed extensive middle cerebral artery (MCA) and posterior cerebral artery (PCA) ischemia on the left. Imaging of the lungs showed bilateral interstitial inflammatory changes. Echocardiography and abdominal ultrasound were without pathological changes. Family history was negative for thrombotic defects and testing for genetic predisposition is still ongoing.
Conclusion: SARS-CoV-2 has been shown to cause thrombotic vascular events than other coronavirus and seasonal infectious diseases. Globally, the majority of thrombotic events reported during a SARS-CoV-2 infection are mainly in the middle-aged and elderly population with concomitant cardiovascular and metabolic diseases. We report a rare case of ischemic stroke in childhood as a complication of SARS-CoV-2.
Disclosure: Nothing to disclose.

EPO-705

Abstract withdrawn

EPO-706

Gender differences and risk factors in intravenous thrombolysis; a year experience in Albania

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Background and aims: Intravenous thrombolysis with alteplase is the mainstay treatment for ischemic stroke within 4.5 hours of symptom onset in ischemic stroke. This is a cohort retrospective study that took place from January 2019 to January 2020 which aims to assess outcomes using NIHSS based on age and sex.
Methods: We enrolled 122 patients with ischemic stroke who had a normal CT scan and were within 4.5 hours of symptom onset as per guidelines. The patients were evaluated with the NIHSS on admission and on discharge from the hospital and the t-test was used to compare both sexes and age (65 being the cutoff). We also reviewed risk factors such as hypertension, diabetes mellitus, atrial fibrillation, if they were present on our patients and compared those based on sex and age using the Chi-squared and Fischer's exact test.
Results: Patients ranged from 36 years of age to 81 with the mean age being 65.4 (SD=9.7). Men were younger than women (mean of 63 compared to 68.4; $p<0.01$). When comparing patients based on age (> or <65) there was a statistical difference regarding hypertension as a risk factor. NIHSS on admission ranged from 6–24 for both sexes with a mean of 15.1 (4.6) for females and 14.9 (4.0) for males. On discharge the NIHSS ranged from 0–23 in females with a mean of 9.4 (5.7) and from 1–24 in males with a mean of 9.9 (5.8).
Conclusion: The outcomes of stroke patients undergoing thrombolysis vary on age but doesn't seem to vary based on sex.
Disclosure: Nothing to disclose.

EPO-707

Mean platelet volume (MPV) predicts large vessel occlusion and ischemic stroke outcome

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Department of Neurology Military Institute of Medicine, Warsaw, Poland

Background and aims: Early diagnosis of large vessel occlusion (LVO) is crucial in pre-hospital management of acute ischaemic stroke (AIS). Biomarkers as predictors of LVO and stroke outcome remains unknown. MPV is a surrogate marker of activated platelets and is considered a link between inflammation and thrombosis. We hypothesized that high MPV may be associated with LVO and may predict worse AIS outcome.
Methods: This was a retrospective study of 361 patients with AIS who were treated with thrombolysis and/or mechanical thrombectomy in a tertiary stroke centre between 2011–2019. 124 patients (34.3%) had mechanical thrombectomy and 32 patients (25%) received bridge thrombolysis.
Results: The mean MPV in the cohort was 9.86±1,5 fL first quartile <8.8 fL, second 8.8–9.9 fL, third 9.9–10.8 fL, forth >10.80 fL). Patients in the forth quartile compared to the first had more frequently LVO (respectively 58% vs. 31%, p=0.01). There was a relation between MPV quartiles and risk of independence (mRS 2) at discharge (RR 0.71; 95%CI 0.58–0.86), and linear relation between MPV and baseline NIHSS and door-to-need time (respectively R=0.2; R= -0.21; p<0.01).
Conclusion: MPV may serve as a novel index of LVO and predicts unfavorable stroke outcome in AIS patients treated with reperfusion therapy.
Disclosure: This paper was prepared without any external funding source. The authors have no conflicts of interest to declare.

EPO-708

Cerebral infarction and sildenafil use: a casual or causal relationship?

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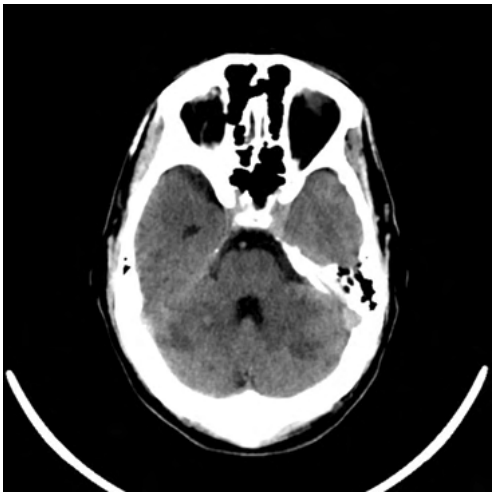
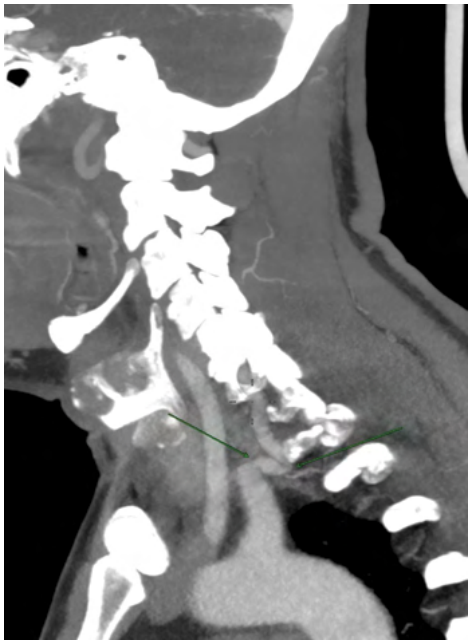
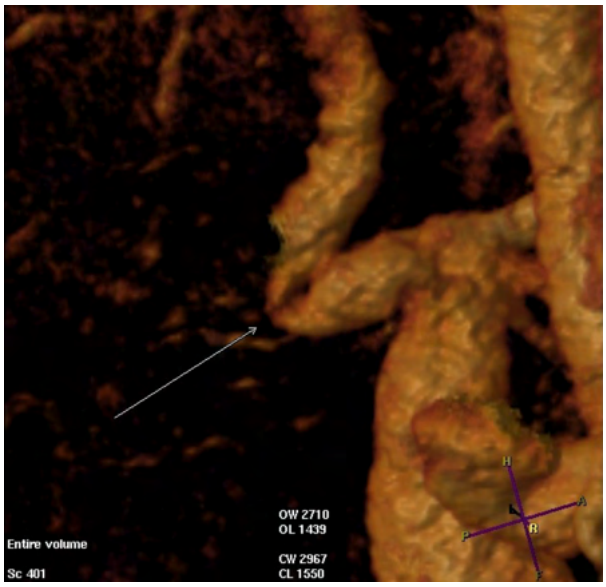
Background and aims: The association between sildenafil use and cerebral ischemia is unusual. We present the case of a young patient who developed an infarction in the vertebrobasilar territory after sildenafil ingestion and we analyze the possible mechanisms involved.
Methods: A 47-year-old man with no medical history presented acute dizziness and vomiting one hour after taking alcohol and 50mg of sildenafil, subsequently falling asleep. Upon awakening, he presented incoordination of all four limbs, double vision and difficulty speaking.
Results: On admission to the emergency department, 17 hours after clinical onset, the neurological examination revealed severe dysarthria, left internuclear ophthalmoplegia and ataxia of the four limbs. Cranial CT scan showed ischemic lesions in both cerebellar hemispheres and left hemiprotuberance. CT angiography revealed a hypoplastic right vertebral artery terminating in posterior inferior cerebellar artery and a dominant left vertebral artery, presenting a loop with two focal stenosis in its origin. The etiological study of infrequent causes of stroke in young adults and a complete cardiological study showed no significant findings. The causal relationship between sildenafil and stroke is controversial, mechanisms involved have not been clarified yet. Hemodynamic alterations due to sustained hypotension or the appearance of drug-induced paroxysmal atrial fibrillation have been proposed.



Cranial CT scan showing bilateral hypodense cerebellar lesions.



CT Angiography showing a loop with two focal stenosis in left vertebral artery origin.



CT Angiography reconstruction. Detail of left vertebral artery origin.

Conclusion: In this case, a causal relationship between sildenafil intake and multiterritorial infarction is likely due to a hemodynamic mechanism associated with vertebral artery stenosis.
Disclosure: Nothing to disclose.

Epilepsy 4

EPO-709

Paroxysmal dystonia: a vascular event or epileptic seizure

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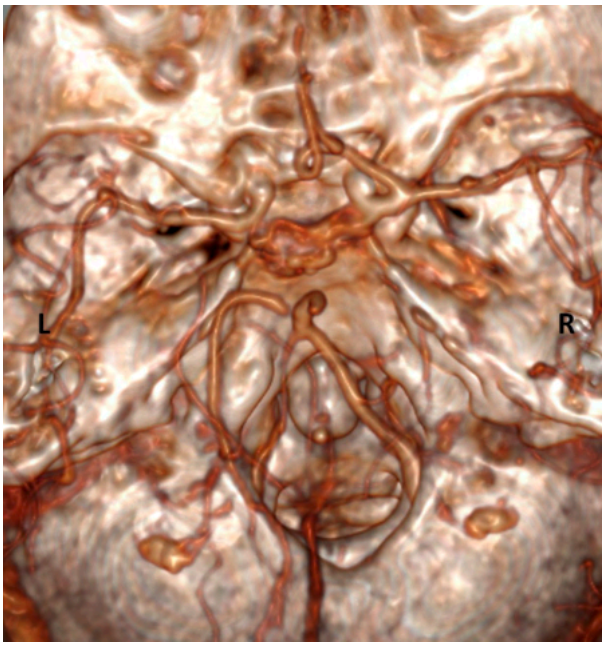
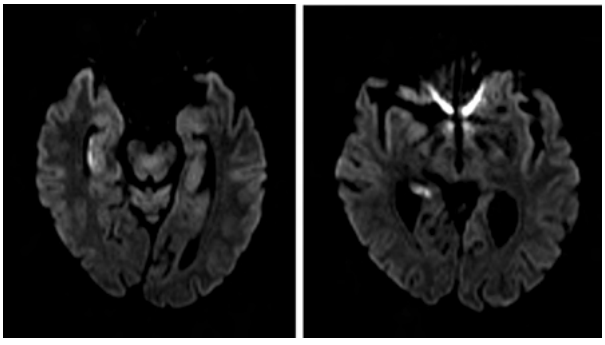
Background and aims: Dystonia represents a diagnostic challenge, due to its various aetiologies. Stroke affecting basal ganglia or thalamus is one of its known causes. Medial temporal lobe seizures may also cause dystonic posturing contralateral to epileptogenic zone, with ipsilateral head deviation and amnesia.
Methods: .
Results: Clinical Case: A 75-year-old male with vascular risk factors presented with a sudden onset of blurred vision and vomiting. The neurological examination revealed strabismus, central left facial palsy, dysarthria, left hemiparesis and tacto-algic hypoesthesia (NIHSS 13). He also presented paroxysmal and stereotyped episodes of left's arm dystonic posturing and right cephalic rotation. CT-angiography revealed occlusion of the top of the basilar artery and thrombolysis with alteplase was initiated. He was also treated with levetiracetam without resolution of the seizure-like episodes. On admission to another hospital, according to the drip-and-ship approach, a significant improvement occurred (NIHSS 3). Neuroimaging studies demonstrated patency of the basilar artery, persisting an occlusion of the right posterior cerebral artery on its P3 segment. Hours later, an unremarkable neurological examination was noted, except for amnesia for the episode. MRI revealed restricted diffusion in the right hippocampus.



Occlusion of the top of the basilar artery


MRI revealed restricted diffusion in the right hippocampus

Conclusion: We present a case of posterior circulation stroke in combination with arm dystonia and cephalic rotation, an interesting phenomenology with a challenging aetiological diagnosis. Despite the potential of thalamic hypoperfusion causing dystonia, both semiology and MRI changes suggest that it was probably a result of an acute symptomatic seizure originated in the hippocampus, in the context of an ischaemic stroke.
Disclosure: Nothing to disclose.

EPO-710

Oxcarbazepine as the initial monotherapy of focal epilepsy: Focus on epileptiform activity index

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Department of Neurology, Moscow, Russian Federation

Background and aims: Oxcarbazepine (OXC) has been used in Russia since 2007. Our study is aimed to assess OXC effectiveness, tolerability, and epileptiform activity index (EAI) changes when used as the initial therapy of newly diagnosed focal epilepsy.
Methods: 89 patients aged 15–75 with newly diagnosed focal epilepsy were involved in our study. Each of the patients was evaluated at baseline, as well as on 1, 3, 6, and 12 months of treatment. Patients were separated into three groups according to the OXC dose they received: less than 1,200mg/day, 1,200mg/day, above 1,200mg/day. OXC tolerability was evaluated using SIDAED scale (Side Effects of Anti-Epileptic Drugs).
Results: Percentage of patients kept OXC monotherapy in 12 months is 71.9% (64 patients), among them: 52.9% took 1,200mg/day, 12.3% – less than 1,200mg/day, 6.7% – above 1,200mg/day. Adverse events were reported in 9.0% of cases (8 patients). In 12 months total EAI was reduced by 2.5 times showing the effectiveness of the therapy.
Conclusion: OXC showed itself as a highly effective and tolerable medicinal product for focal epilepsy initial monotherapy. Total EAI 2.5-fold reduction allows its usage as an additional objective indicator of OXC therapy effectiveness.
Disclosure: The authors have nothing to disclose.

EPO-711

Role of High resolution MRI in Mesial Temporal Lobe Epilepsy

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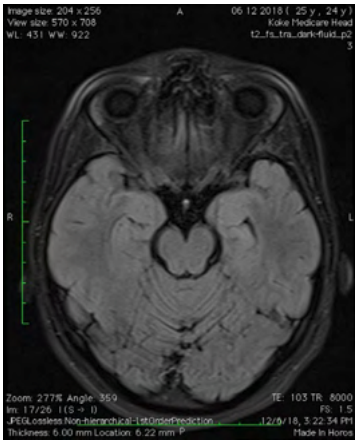
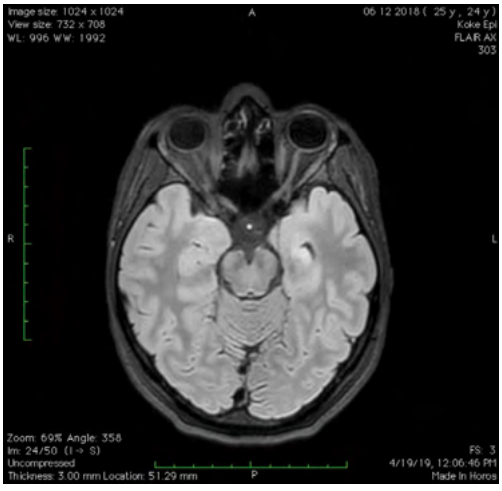
Background and aims: Mesial Temporal Lobe Epilepsy(MTLE) is the most common pharmaco-resistant epilepsy where surgery has an important role.
Methods: A multidisciplinary team co-ordination between different neuroscientists including psychiatrists and psychologists is needed to effectively correlate all the clinical, pathological, electrophysiological and radiological data to better manage patients with refractory epilepsy. Patients with MTLE usually remain seizure free after surgical resection. We present a case of MTLE where 1.5 Tesla MRI showed no changes in mesial structures.

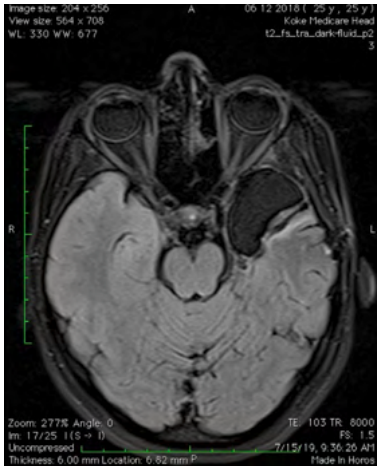


Axial 1.5 Tesla MRI before intervention showed no evident lesions in left mesial temporal lobe



Axial sections in 3.0 Tesla MRI - FLAIR sequences of the left hippocampal structures showed a hypersignal and hippocampal volume loss in quantitative analysis resulting in an asymmetry between the two mesial temporal lobes

Results: Based on the strong suspicion of temporal lobe asymmetry due to the correlation between the typical ictal semiology and the electrophysiological changes in Video EEG a 3.0 Tesla MR was performed that clearly evidenced the asymmetry due to the hippocampus neuronal loss.



Axial sections in 3.0 Tesla MRI – FLAIR sequences of the left hippocampal structures post-op cavity.

Conclusion: This case shows the value of higher resolution imaging techniques in MTLE for quantitative analysis of the mesial structures in typical clinical-electrophysiological cases of MTLE where 1.5 T MR shows no evident lesion.
Disclosure: Nothing to disclose.

EPO-712

Psychometric properties of HADS-A in Russian patients with epilepsy

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Background and aims: Generalized anxiety disorder (GAD) is one of the most common mental disorders in persons with epilepsy (PWE), with a prevalence rate of 10.2% (Scott AJ et al, 2017). Its early detection is essential for maintaining the well-being and work productivity in PWE. The anxiety subscale of the Hospital Anxiety and Depression Scale (HADS-A) was found in several studies to be an effective and reliable screening tool for anxiety disorders in PWE. To date, HADS-A was not studied in Russian PWE.
Methods: We aimed to investigate the Russian version of HADS-A as a GAD screening instrument in PWE. A consecutive cohort of PWE was assessed with GAD Module of the Mini International Neuropsychiatric Interview (MINI) and the HADS-A. Demographic and clinical variables were collected. Receiver operating characteristic (ROC) analyses for HADS-A scores, with the identification of higher Youden's index was used as statistical methods.
Results: The cohort consisted of 233 PWE: 152 (65.4%) female; mean age was 41.1 (14.7); 213 (91.4%) had focal epilepsy; mean age at onset of the epilepsy was 24.8 (16.8), 61 (27.5%) had GAD. ROC analysis showed that HADS-A had an area under the curve of 0.862 (95%CI 0.811–0.913), a sensitivity of 70.1% (95%CI 57.6–81.1), a specificity of 86.3% (95% CI 80.3–91.2), a positive predictive value of 36.7 (95%CI 27.8–46.7), a negative predictive value of 96.3 (95% CI 94.6–97.4), and the largest Youden index of 0.5670 for a cutoff score of >10.
Conclusion: The Russian version of HADS-A has modest efficacy in detecting GAD in PWE.
Disclosure: The authors have nothing to disclose.

EPO-713

Alcohol withdrawal seizures: a retrospective study of the risk of relapse

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Background and aims: Alcohol withdrawal seizures (AWS) usually occur 6–48 hours after the intake reduction. They are considered acute symptomatic seizures, usually not requiring specialised follow-up after a control EEG and CT.
Methods: This retrospective study was conducted on patients admitted to the emergency department after AWS between 01.01.2013–14.12.2018 and for whom an EEG was requested. 149 patients were enrolled; for each, previous AWS and relapses were researched until 01.12.2020. We compared characteristics of the 16 patients with (A) and the 133 without (B) relapses in the follow-up (significance level=0.05).
Results: The mean age was 53.3 years, 79% were male. Cirrhosis was present in 13.4%, hyponatremia (<135mmol/l) in 22.3%, mean MCV was 95 fl (normal range 82–98), mean gamma-GT was 444 U/L (normal range 9–40). Brain CTs (n=138) showed pathologic and often overlapping findings in 34% (traumatic sequelae in 7, bleedings in 14, atrophy in 34), without difference between groups. 12 patients showed epileptogenic anomalies in the EEG, which were more frequent in group A (p=0.058). 11% patients had one or more relapses after the index event, after a median time of 376 days, especially if they had a history of AWS (p=0.0036). Active benzodiazepine treatment prior to admission was more prevalent in group (B) than in group (A) (p=0.052).
Conclusion: AWS seem to occur mostly in middle-aged males, in particular with a history of AWS. Acute or chronic CT abnormalities were noted in one third. The recurrence risk of 11% may require longer driving restrictions. Benzodiazepine treatment reduces the risk of AWS.
Disclosure: Nothing to disclose, MS and SV have shares in epilog.

EPO-714

Neurological complications and EEG findings of inadvertent intrathecal injection of Tranexamic Acid – Case Report

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Background and aims: Tranexamic Acid (TXA) is being widely used during surgery to reduce bleeding. Packaging similarities have led to accidental intrathecal injections being reported, some with fatal outcomes. We present two cases of inadvertent intrathecal injection of TXA with neurological and neurophysiological correlation.
Methods: Case Report.
Results: 1. A 73-year-old man underwent spinal anesthesia for a knee surgery. Instead of bupivacaine, he received TXA intrathecally (dose unknown). Immediately after, the patient reported severe burning pain in perineal region and lower limbs. A general anesthesia with propofol, remifentanil and rocuronium was induced due to hemodynamic instability, propriospinal myoclonus and spinal segmental myoclonus, involving mainly the abdominal region (video1). Electroencephalogram (EEG) showed burst-suppression pattern with multifocal electrographic seizures. Midazolam and Levetiracetam were added with myoclonus remission and seizure control. The patient was extubated three days later and progressively improved to full recovery. 2. A 19-year-old male received TXA (250mg) instead of bupivacaine intrathecally by mistake, during sacrococcygeal epidermoid cyst surgery. The patient reported immediate perianal burning pain, followed by exuberant propriospinal myoclonus (video2). He was intubated and mechanically ventilated, with propofol plus midazolam. He received levetiracetam, valproate, diazepam and morphine without improvement. Rocuronium was needed to suppress involuntary movements. EEG revealed occasional spikes on temporal regions. After three days he was weaned off sedation, still presenting exuberant shivering episodes with preserved awareness (video3), but progressing to full recovery without neurological sequelae.
Conclusion: Polymyoclonus, radicular pain and seizures are possible complications of intrathecal TXA administration. Rapid recognition and multidisciplinary approach lead to a better prognosis.
Disclosure: No disclosures.

EPO-715

Refractory post hypoxic myoclonus: from Myoclonic Status Epilepticus to Lance-Adams Syndrome

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Background and aims: Post-hypoxic myoclonus (PHM) is a consequence of severe hypoxic-ischaemic brain injury. Myoclonus status epilepticus (MSE) and Lance Adams Syndrome (LAS) are the acute and chronic forms of PHM presentation, respectively. Differentiating these two entities is important given their different prognosis and approaches, but particularly challenging in patients under sedation.
Methods: Case report.
Results: We report a case of a 53 old man who presented generalized myoclonus after a hypoxic event following a removal of thyroglossal cyst that complicated into a cervical haematoma. Clinically progression and sequential electroencephalograms (EEG) showed a progression from MSE to LAS. EEG showed a progression from burst suppression pattern into generalized periodic discharges while sedated, typical of MSE, followed by polyspike activity, when weaned off the sedation, featuring LAS. Neuroimaging disclosed no specific abnormalities. Response of treatment was poor, besides several anti-epileptic drugs adjustments and physical therapy, conditioning prolonged hospitalization, and severe disability. Zonisamide showed to be partially effective.
Conclusion: Our case highlights the clinical and neurophysiological development of LAS from MSE as a possible continuum and not two separate entities, as well the therapeutic challenges that it can harbours. The improvement of survival rates after cardiorespiratory events raises the incidence of such severe neurological sequelae and warrants more extensive studies and treatment trials.
Disclosure: Nothing to disclose.

EPO-716

Germline variant of DEPDC5 in focal cortical dysplasia: a case report

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Background and aims: Mutations within genes of the mammalian target of rapamycin (mTOR) pathway are increasingly recognized in focal cortical dysplasia (FCD). The advent of next generation sequencing (NGS) enabled the detection of novel variants in DEPDC5 gene, which acts as a negative regulator of mTOR complex 1, essential to neuronal growth and migration.
Methods: N/A.
Results: An 18-year-old patient that at the age of 12 was diagnosed with focal epilepsy. Interictal EEG showed an intermittent slow in the right occipital region and the video-EEG recorded a paroxysmal arousal followed by a brief asymmetric tonic seizure associated to a focal ictal EEG onset in the right frontal region. Brain MRI showed a right paramedian inferior occipital lesion, characterized by cortical thickening, graywhite matter blurring and an increased T2 signal of the subcortical white matter with transmantle sign, probably corresponding to FCD type II. The patient was also diagnosed with attention-deficit/hyperactivity disorder (ADHD) and mild intellectual disability (ID). Targeted NGS detected a heterozygous germline variant on DEPDC5 (c.3241A>C, p.Thr1081Pro). He was treated with valproic acid and clobazam with seizure freedom.
Conclusion: The index patient had clinical features compatible with DEPDC5 phenotype (FCD, focal epilepsy, ADHD and ID). The identified missense variant, located at 22q12.3 in a coding region of exon 32, has previously been reported in two other epileptic patients. Although interpretation of missense variants remains a challenge, DEPDC5 variants in patients with FCD cannot be neglected, since it may have important treatment implications in the future, namely the use of mTOR inhibitors.
Disclosure: Nothing to disclose.

EPO-717

Vagus Nerve Stimulation (VNS) in a Refractory Epilepsy Center: our experience

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Background and aims: VNS is a treatment option in refractory epilepsy, allowing to decrease frequency and intensity of seizures. We aim to characterize the population of epileptic patients treated with VNS in a Refractory Epilepsy Center, the outcome and predictors of response.
Methods: Retrospective study of consecutive patients submitted to VNS between 2012 and 2020, followed in our outpatient clinic. Univariate analysis was performed to compare the group of patients with good response (A: reduction in seizure frequency of at least 50%) with the group of non-responders (B). Binary logistic regression was then performed to assess any independent predictors of response to VNS.
Results: 33 patients were included (13 of pediatric age), median age of 28 years, 39.4% male (n=13). Median time of disease duration was 17.7 years and median follow-up time in outpatient clinic was 2.96 years. At the time of surgery, 90.6% were under three or more antiepileptic drugs. In our population, 53.3% were responders (group A) and 28.6% of patients from group B reported subjective improvement with some reduction of seizure frequency. Group A had more frequently multifocal epilepsy (A:65.3%, B:15.4%, p=0.02). Multivariate analysis was performed and only multifocal epilepsy emerged as the only independent predictor of response to VNS (OR 9.2, IC 95%: 1.5–56, p=0.017).
Conclusion: In our patients, VNS showed to be an effective treatment, with findings and outcomes in line with previous studies. Mechanisms of neuromodulation not yet understood could justify a better response in multifocal epilepsy. VNS remains a promising treatment option in patients with refractory epilepsy.
Disclosure: Nothing to disclose.

EPO-718

Creutzfeldt-Jakob Disease – a single center study

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Background and aims: Creutzfeldt-Jakob (CJD) disease is a progressive, fatal neurodegenerative disorder, caused by the prion protein. Due to a long asymptomatic period and nonspecific nature of early symptoms, diagnosis is often difficult and the disease is still underreported in Poland.
Methods: The aim of this study was to describe the clinical, radiological and electroencephalographic characteristics of patients with CJD, hospitalized in the University Hospital in Krakow. This was a retrospective, hospitalbased study.
Results: We retrospectively reviewed the medical records of 20 patients (13 females). Mean age of patients was 61.4 years (SD±12,8; range: 34–79). The most common clinical symptoms was dementia (20/20), followed by pyramidal or extrapyramidal signs (17/20), cerebellar or visual deficits (13/20) and akinetic mutism (9/20). Mean time interval between onset of clinical manifestation and diagnosis was 4,7 months (range 1–12). Characteristic abnormalities in brain MRI were found in 14 cases (77% out of 18). Classical electroencephalogram (EEG) changes of periodic triphasic waves were seen in 18 patients (90%). In 10 cases (out of 16) the CSF 14-3-3 protein assay was positive. CSF-RT-QuIC test was performed in three patiens (1 positive). 16 cases were diagnosed as probable CJD and four were definite CJD (1 brain biopsy, three autopsies).
Conclusion: Progressive cognitive decline is the most common symptom in CJD. Characteristic abnormalities in MRI and EEG are seen in the vast majority of patients. A strong clinical suspicion aided by characteristic brain MRI and EEG abnormalities is essential for timely diagnosis.
Disclosure: Nothing to disclose.

EPO-719

Teratogenic influence of using antiepileptic drugs during the pregnancy on the intellectual development of a child

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Background and aims: We studied the long-term effects of teratogenic influence on the cognitive development of the child. The study involved 80 people: 40 mothers with epilepsy and 40 children aged three to nine years.
Methods: To diagnose the development of children, the Wechsler WSIC Intelligence Scale for Children. Data on the clinical condition of the mother during pregnancy and childbirth were also collected. Statistical processing of the results included frequency analysis, comparison of samples by the Mann-Whitney U-test, analysis of variance, correlation and regression analysis.
Results: The study showed that intellectual development of children is affected by the form of mother's epilepsy, antiepileptic drugs taken by her, the preparedness of childbirth, the presence of seizures during pregnancy, complications of pregnancy, the way of parturition and the type of feeding.
Conclusion: The most important factors for reducing the impact of teratogenic effects were the preparedness of the birth, the absence of seizures during pregnancy and the absence of complications of pregnancy.
Disclosure: Nothing to disclose.

EPO-720

Novel Device for ultra-long-term electroencephalographic monitoring

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Background and aims: Electroencephalographic (EEG) monitoring is used by clinicians to help capture neural abnormalities in conditions such as, epilepsy, sleep disorders, encephalitis, and stroke. These signals are quite small 100 V when measured on the scalp, and about 1–2 mV when measured on the brain surface. Because of their low amplitude especially on the scalp, the measurement of EEG is more difficult than other bio-signal measurements such as electrocardiogram (ECG). The current gold standard in epilepsy diagnosis and monitoring is video and10–20 scalp EEG recordings in a hospital or outpatient setting. However, the maximum recording time is typically 1–2 weeks. We have developed a new sub scalp device called Minder, capable of significantly extending the data capture period and providing clinicians with more information to aid diagnosis and management.
Methods: Minder's recording electrodes are implanted subcutaneously under the scalp but above the bone, providing a stable low-impedance signal. Unlike other sub scalp systems, the Minder system uses a multichannel electrode lead that is placed across the skull allowing the recording of EEG signals from both hemispheres of the brain. EEG recordings from the Minder device were compared to the gold standard.
Results: We were able to record long-term signals. Minder recordings were able to identify clinically important EEG signals including physiological, interictal epileptiform discharges, seizure activity, and sleep architecture.
Conclusion: We have described an ultra-long-term EEG recording system that will enable clinicians to collect EEG data from patients for greater than 14 days potentially improving the diagnosis and management of epileptic disorders.
Disclosure: Some of the authors declare that they have personal financial interests.

EPO-721

Epilepsy: a look at the national public expenditure in the last five years

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Background and aims: Epilepsy is a chronic disorder, the hallmark of which is recurrent, unprovoked seizures. Is stimulated that 65 million people around the world have epilepsy. In Brazil, the estimate is that one person for every 2,000 people, have epilepsy. Therewith, epilepsy it's a disease that should be studied and have a very important roll in Brazilian's public health.
Methods: This is an observational, retrospective, cross-sectional study. The collected data was through SUS Hospital Information System (SIH/SUS), in DATASUS (Department of Informatics of the Brazilian Health System) collected on September 24th of 2020 – four-years time analysis (from July 2016 to July 2020). The variables analyzed were: Age Group, AIH (Hospital Admission Authorization), Total cost, Year of occurrence and Federation Units.
Results: There were 266,677 hospitalizations for epilepsy in Brazil in the last five years, representing a cost in excesso of 200.000,000 reais to public coffers. Investigating the regional scenarios, it was noted that the Southeast had a higher prevalence of hospitalizations (41,5%), consequently being responsible for 49,5% of national expenses, followed by the Northeast, with 23,4% of hospitalizations and 18,5% of expenses and by the South with 21,5% of hospitalizations and 21,2% of costs.
Conclusion: It is concluded that epilepsy is a chronic disorder which affects a part of the Brazilian population and has substantial costs to public accounts, has an elevated number of hospitalizations with southeast region highlighted for most hospitalizations and costs to public healthcare.
Disclosure: There are no conflicts of interest.

EPO-722

Levels of IL-1beta, TNF, BDNF and NTRK-2 in the blood serum of patients with temporal lobe epilepsy

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Background and aims: Based on a number of clinical and basic studies, there is evidence of the presence of an inflammatory and neurogenesis processes in TLE.
Methods: We studied the concentration of BDNF, TNF, NTRK-2, IL-1B in blood plasma in 34 patients (60% – women and 40% – men, average age – 41 years), and in 24 healthy people who make up the control group (62.5% – women and 37.5% – men, average age-27 years) using ELISA. The Mann-Whitney criterion was chosen by statistical analysis. The differences were considered statistically significant at $p<0.05$.
Results: We found a statistically significant decrease in BDNF levels ($p=0.05$), as well as TNF ($p=0.05$) in peripheral blood in patients with TLE compared to healthy people. In the group of patients with TLE, the concentration of BDNF was 52.2±13.9 ng/mL. In the control group, the BDNF level was 97.9±11.7 ng/mL. In the group of patients with TLE, the TNF concentration was 45.9±9.7 pg/mL. In the control group, the TNF level was 89.05±15.4 pg/mL. We didn't found statistically significant differences in the comparison groups for NTRK-2 and IL-1B, ($p=0.05$).
Conclusion: We were found statistically significant decrease in the concentration of BDNF in peripheral blood in patients with TLE.
Disclosure: No conflict of interest.

Headache and Pain 4

EPO-723

Idiopathic intracranial hypertension and Anemia: is it a predictor of a better prognosis?

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Background and aims: Idiopathic intracranial hypertension (IIH) is a complex disease, mostly affecting young obese women. It usually leads to a severe headache and a permanent visual impairment. Several etiologies were related to IIH, especially anemia. However, it is frequently under-estimated. Herein, we aimed to assess the clinical features of anemia associated IIH and compare them with patients without anemia (PWA).
Methods: A retrospective study was performed including patients with presumed IIH (according to Modified Dandy's criteria) referred to our department of neurology over six years [2015–2020] to describe clinical features and neuroradiological findings in patients with IIH and anemia and compare them with PWA.
Results: A total of 67 patients with IIH were enrolled (M/F:1/66), which included 19 patients with anemia (mean age: 31,9±12,1 years) and 48 PWA (mean age: 30,7±9,9 years). Compared to PWA, the anemia group had a longer diagnostic delay and tended to present visual disturbance rather than nausea and vomiting. Their most common imaging sign was transversal sinus stenosis, whereas, it was empty sella for PWA. At baseline, both groups had the same mean CSF opening pressure (p=0,636). After treatment, the outcome was nearly the same in terms of the evolution of clinical signs (p=0,187), the number of lumbar puncture decompression (p=0,608), and papilledema grade in follow-up (p=0,731).
Conclusion: through this study, we highlight the importance of considering anemia as a cause of IIH when headache and visual impairment are presented and carefully treating it to improve the outcome of these patients.
Disclosure: Nothing to disclose.

EPO-724

Atogepant Improved Patient Functioning Using MSQ v2.1 in a 12-Week Phase 3 (ADVANCE) Trial for Migraine Prevention

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Background and aims: Atogepant is an oral calcitonin gene–related peptide receptor antagonist being developed for preventive migraine treatment.
Methods: This phase three, multicenter, randomized, double-blind, 12-week, placebo-controlled ADVANCE (NCT03777059) trial evaluated efficacy and safety of atogepant 10mg, 30mg, or 60mg, or placebo once daily for preventive migraine treatment in participants with 414 migraine days/month. The Migraine-Specific Quality of Life Questionnaire version 2.1 (MSQ v2.1) Role Function-Restrictive (RFR) change from baseline to week 12 was a secondary outcome. Least squares mean differences (95% CI) vs placebo were reported for change from baseline at weeks 4, 8, and 12 in the MSQ v2.1 RFR, and Role Function-Preventive (RFP) and Emotional Function (EF).
Results: Of 910 participants randomized, 902 received treatment (mean age: 41.6 years; 89% female); 873 were included in the modified intent-to-treat population: atogepant 10mg, n=214; 30mg, n=223; 60mg, n=222; placebo, n=214. At week 12, significant and clinically meaningful improvements for all atogepant groups vs placebo were observed on the RFR (10mg, 9.9 [5.5–14.4]; 30mg, 10.1 [5.7–14.5], 60mg, 10.8 [6.4–15.2]), RFP (10mg, 5.8 [1.9–9.6]; 30mg, 6.9 [3.1–10.7]; 60mg, 7.1 [3.3–10.9]), and EF domains (10mg, 8.3 [3.4–13.1]; 30mg, 9.7 [4.9–14.4]; 60mg, 10.5 [5.8–15.3]). Significant differences vs placebo were observed at the earliest time point (week 4) and throughout the treatment period. All atogepant groups achieved within-group minimally important difference among the MSQ v2.1 domains at weeks 4, 8, and 12.
Conclusion: Atogepant demonstrated significant and clinically meaningful between- and within-group reductions in emotional impact and improvements in functioning in daily social and work-related activities.
Disclosure: This study was supported by Allergan (prior to its acquisition by AbbVie.

EPO-725

OnabotulinumtoxinA Treatment Satisfaction among Patients with Chronic Migraine

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Background and aims: Limited research exists on outcomes indicative of satisfaction with onabotulinumtoxinA treatment among patients with chronic migraine (CM). The study objective was to evaluate onabotulinumtoxinA treatment satisfaction using a novel, composite outcome measure (COM).

Methods: Descriptive analysis of the 2017/2018 Adelphi Migraine Disease-Specific Programme; a point-in-time survey of physicians and their patients with migraine, was performed using pooled data for UK, Germany, France, Spain, Italy, USA, Japan, and Brazil. For this study, patients with CM with current or past onabotulinumtoxinA use were identified. Treatment satisfaction was assessed by a COM (yes/no), defined as whether/not patients met one of the following criteria for onabotulinumtoxinA: discontinued for negative reason; current preventive treatment issue reported; physician/patient treatment satisfaction rating of not satisfied; concurrent preventive treatment use. Treatment satisfaction rates were then calculated. In a sensitivity analysis, onabotulinumtoxinA was evaluated as monotherapy.

Results: Of 148 patients (mean age 45.54 years [standard deviation (SD) 11.22]; female 81.8%), the mean number of previous preventative treatments was 2.27 (SD 0.95) and almost 1/3rd (32.4%) used onabotulinumtoxinA in combination with another preventive treatment. Per the COM, 62.2% of patients were not satisfied with onabotulinumtoxinA treatment. When explored as a monotherapy, half of patients (48.0%) were not satisfied. Of those who provided information on physician visits for onabotulinumtoxinA treatment (n=14), four patients (28.6%) stated that they had missed appointments.

Conclusion: Findings from a novel COM indicated that at least half of patients/physicians treated with onabotulinumtoxinA were not satisfied with the treatment for CM, highlighting an unmet need in this population.

Disclosure: This study was sponsored by Eli Lilly and Company, Indianapolis, Indiana, USA.

EPO-726

Pooled analysis of changes in heart rate and blood pressure with fremanezumab in migraine patients

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Background and aims: The randomized, double-blind, placebo-controlled, phase three studies (2 HALO studies and FOCUS) have evaluated fremanezumab, a fully-humanized monoclonal antibody (IgG2a) that selectively targets calcitonin gene-related peptide (CGRP), for preventive treatment of episodic and/or chronic migraine in adults. This pooled analysis of data from those three studies evaluated changes in heart rate (HR), systolic blood pressure (SBP), and diastolic blood pressure (DBP).

Methods: Across all three studies, patients were randomized (1:1:1) to quarterly fremanezumab, monthly fremanezumab, or matched monthly placebo for 12 weeks of double-blind (DB) treatment. In this pooled analysis, changes from baseline in HR, SBP, and DBP at the end of the DB treatment period for migraine patients were summarized descriptively.

Results: Across the phase three studies, 1,897 patients received fremanezumab (quarterly, n=943; monthly, n=954) and 945 received placebo. At the end of 12 weeks of double-blind treatment, mean (SE) changes from baseline in HR (measured in beats per minute), as well as SBP and DBP (measured in mmHg), were small and similar across groups (Table).

Mean (SE) change from baseline	Quarterly fremanezumab (n = 943)	Monthly fremanezumab (n = 954)	Placebo (n = 945)
HR (bpm)	0.4 (0.32)	0.4 (0.33)	0.0 (0.32)
SBP (mmHg)	−0.7 (0.39)	−0.8 (0.39)	−0.5 (0.38)
DBP (mmHg)	−0.3 (0.28)	−0.5 (0.29)	−0.8 (0.30)

HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; SE, standard error; bpm, beats per minute.

Table. Changes from Baseline in HR, SBP, and DBP Over 12 Weeks of Double-blind Treatment

Conclusion: This pooled analysis showed that, at the end of 12 weeks of DB treatment, fremanezumab treatment resulted in minimal increases in HR and decreases in SBP and DBP from baseline that were not clinically significant and were comparable to those observed in the placebo group.

Disclosure: These studies and analyses were funded by Teva Pharmaceuticals.

EPO-727

A retrospective database study of migraine epidemiology in southern Israel

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Background and aims: Migraine is a common neurological disease, with an age-standardized prevalence of 14.4% worldwide (GBD 2016 Headache Collaborators. Lancet Neurol. 2018;17:954–976). The introduction of new migraine-specific therapeutic modalities emphasizes the need for epidemiological data on migraine at the national and regional level that will enable decision-makers to identify data-supported policies and resource allocation. In this study, we evaluated epidemiology of migraine in the southern district of Israel, using the electronic medical records (EMR) database of the largest Israeli Health Maintenance Organization (HMO).

Methods: In this population-based retrospective, observational, cohort study, adult migraine patients were identified in the computerized database of the southern district of the "Clalit Health Services" HMO (total population, 0.75 million). Patients were identified based on recorded diagnosis (ICD-9) and/or claims for specific anti-migraine medication (triptans) during 2000–2018. We calculated the prevalence for 2018 per 10,000 adults.

Results: In 2018, a total of 29,938 migraine patients were identified out of 391,528 adult HMO members. Most of the patients were women (75.8%) and the mean age of diagnosis was 36.94±13.61 years. The overall prevalence of migraine (per 10,000) was 764.64 (7.64%), 1143.34 (11.43%) for women and 374.97 (3.74%) for men. The highest prevalence was observed in patients 50–60 years and 40–50 years (1,143.98 and 1,019.36, respectively) and the lowest prevalence was among patients 18–30 years and over 70 years (433.45 and 398.49, respectively).

Conclusion: This is the first epidemiological study of migraine prevalence in Israel. Compared to international estimations, migraine appears to be underdiagnosed in Southern Israel.

Disclosure: Funded by Teva Pharmaceuticals.

EPO-728

Variability in migraine prevalence in southern Israel communities: a retrospective database study

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Background and aims: Appropriate and timely diagnosis is one of the most important milestones in effective migraine care and may vary by region due to differences in migraine awareness, access to medical care, and local healthcare systems. The purpose of this study was to quantify variability in migraine diagnosis rates across different communities under universal national health coverage.

Methods: In this population-based retrospective, observational, cohort study, adult migraine patients were identified in the computerized database of the southern district of the "Clalit Health Services" Health Maintenance Organization (HMO) based on recorded diagnosis (ICD-9) and/or claims for specific anti-migraine medication (triptans). Migraine prevalence in 2018 was calculated in the entire population and across different individual municipalities from the HMO database. We utilized a standardized mortality ratio (SMR; standardized for age and gender) approach for comparison among the municipalities.

Results: In 2018, a total of 29,938 migraine patients were identified out of 391,528 adult HMO members. The overall prevalence (per 10,000 adults) of migraine was 764.64 (7.64%), 1,143.34 (11.43%) for women and 374.97 (3.74%) for men. Among the municipalities, adjusted prevalence ranged from 386.14 (3.86%) to 1,320.59 (13.20%). The female-to-male ratio ranged from 1.18:1 to 5.1:1. Prevalence rates were positively associated with the socioeconomic status of the municipalities (spearman rho=0.472, p= 0.006).

Conclusion: Extreme variability in the prevalence of diagnosed migraine suggests underdiagnosis in some municipalities. Resources for awareness or educational programs for patients and providers should be directed towards low prevalence communities to ensure adequate access and treatment of migraine.

Disclosure: Funded by Teva Pharmaceuticals.

EPO-729

Prescription opiate use in patients with migraine in southern Israel: a retrospective database analysis

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Background and aims: Although prescription opiates are not indicated for acute or preventive migraine treatment, they are often prescribed for migraine. This study investigates opiate prescribing rates for migraine patients versus matched controls.
Methods: In this population-based retrospective, observational, cohort study, adult migraine patients were identified in the computerized database of the southern district of the "Clalit Health Services" Health Maintenance Organization (HMO) in Israel. Patients were identified based on recorded diagnosis (ICD-9) and/or claims for specific anti-migraine medication (triptans) during 2000–2018 and matched to non-migraine subjects by gender, age, and primary clinic. Opiate prescribing rates were evaluated during 2018.
Results: Overall, 26,475 migraine patients and 51,221 matched controls were included. In 2018, opiate prescriptions were filled by migraine patients nearly twice as frequently as controls: one-month (1,596 [6.0%] vs 1,606 [3.1%]; p<0.001); two-months (619 [2.3%] vs 619 [1.2%]; p<0.001); >3-months (502 [1.9%] vs 485 [0.9%]; p<0.001). During emergency department visits, migraine patients were more likely to receive opiates than controls (1,733 [6.5%] vs 1,879 [3.7%]; p<0.001). In multivariate analysis, older age (odds ratio [OR], 1.02 [95% CI:1.02,1.03]), higher age at diagnosis (OR, 1.01 [95% CI:1.01,1.02]), comorbid depression (OR, 1.48 [95% CI:1.23,1.77), anxiety (OR, 1.19 [95% CI:0.96,1.47]), fibromyalgia (OR, 3.47 [95% CI:2.99,4.04]), and migraine preventive drug use (OR, 2.36 [95% CI:2.00,2.77]) were associated with opiate prescription.
Conclusion: Although we cannot establish that opiates were prescribed for migraine, these results show that migraine patients are frequently prescribed opiates in emergency and ambulatory settings, despite international treatment guidelines advising against prescribing opiates for migraine.
Disclosure: Funded by Teva Pharmaceuticals.

EPO-730

Neurological status in children with back pain associated with the Hypermobility Spectrum Disorder

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Background and aims: The aim of the study is to find changes in the nervous system in children and adolescents with Hypermobility Spectrum Disorder (HSD).
Methods: 860 children and adolescents aged five to 18 years were examined with using neurological and neuro-orthopedic methods.
Results: Results. HSD signs were identified in 586 (68.1%) patients. 274 (46.8%) patients had pain syndrome which was localized in the neck, in 203 (34.6%) cases – back pain; low back pain observed in 109 (18.6%) patients. All patients had vertebral column deformation: scoliosis in 205 (35.0%) patients; scoliosis with impaired posture in 381 (65.0%) patients. Moderate joint hypermobility was observed in 308 (57.5%) cases; severe hypermobility syndrome – in 228 (42.5%) examined patients. For the purpose of detailed study of the neurological aspects of HSD, 130 children and adolescents were selected. Episodic back pain was diagnosed in 54 (41.5%), daily back pain in 76 (58.5%) children. In neurological status - the autonomic dysfunction syndrome was revealed in 75.4% of cases, insufficiency of the oculomotor nerves (pairs III and VI) innervation in 29 (22.3%) and 6 (4.6%) cases, respectively; nystagmus – 28 (21.5%); insufficiency of the facial nerve innervation – 36 (27.7%); tendon reflexes changes (elevation and anisoreflexia) in 32 (24.6%) and 14 (10.8%) cases; instability in the Romberg position – 38 (29.2%); dysdiadochokinesis – 28 (21.5%) cases. Diffuse muscle hypotension syndrome was detected in 79 (60.1%) cases.
Conclusion: Back pain in children with HSD is probably associated with changes in the spine biomechanics and neurological status.
Disclosure: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

EPO-731

Headache in patients aged 65 years in a tertiary hospital

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Background and aims: Headaches are among the most common neurological complaints and are the cause of disability, including at older ages. **Aim:** Description of patients aged 65 years referred to the Neurology-Headache consultation at a tertiary hospital.
Methods: Retrospective analysis of the clinical and demographic characteristics of patients aged 65 years, based on medical records between 2013–2018. Headaches were classified according to the international headache classification (ICHD-3).
Results: From a total of 1,341 patients, 164 patients aged 65 years were identified with headache (126 were women). Their average age, for the first medical appointment, was 73 years. Most patients came from primary health care. In 53 (32.3%) there was a previous diagnosis of headache and 39.6% reported a new-onset headache, after 50 years of age. Regarding the final diagnoses, 89.1% of the patients met the criteria for primary headache (with tension-type headache being the most frequent, followed by migraine and headache in primary stabbing headache); 27.4% fulfilled the criteria for secondary headache (more frequent were medication-overuse headache, headache attributed to rhinosinusitis and headache attributed to cervical structure) and 9.8% had cranial neuropathies or facial pain (trigeminal neuralgia being the most common condition). 50 of them (30.5%) had more than one type of headache.
Conclusion: In our sample, the majority of patients referred to the consultation had a long-standing history of headache, with primary headaches being the most frequent.
Disclosure: Nothing to disclose.

EPO-732

The effect of Erenumab on sick leave days and healthcare visits in patients with migraine in Finland

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Background and aims: Failed prophylactic treatment in patients with migraine is associated with an increase in sick-leaves and healthcare visits. As Erenumab, a calcitonin gene-related peptide inhibitor (CGRPi), decreases headache days, we assessed the impact of Erenumab on sick-leave days and healthcare visits in employed patients with migraine.
Methods: This retrospective study on the database of a private occupational healthcare provider (Terveystalo, Finland) included employed migraine patients with at least one Erenumab prescription. Responders were defined as patients who received at least two Erenumab prescriptions and no other CGRPi during the follow-up, aligned with national reimbursement system requiring a 50 % reduction in monthly migraine days for continuous reimbursement. Changes in overall and headache related sick-leave days and healthcare visits were assessed 12 months before vs. 6–12 months after and 0–12 months after the first Erenumab prescription.
Results: This retrospective study on the database of a private occupational healthcare provider (Terveystalo, Finland) included employed migraine patients with at least one Erenumab prescription. Responders were defined as patients who received at least two Erenumab prescriptions and no other CGRPi during the follow-up, aligned with national reimbursement system requiring a 50 % reduction in monthly migraine days for continuous reimbursement. Changes in overall and headache related sick-leave days and healthcare visits were assessed 12 months before vs. 6-12 months after and 0-12 months after the first Erenumab prescription.
Conclusion: Erenumab treatment is associated with a significant decrease in headache related sick-leave days as well as healthcare visits among occupationally active migraine patients.
Disclosure: This study was funded by Novartis.

EPO-733

Association of polymorphic variants of MTHFR gene with the development of primary headache in adults

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Background and aims: The aim of the study was to identify genetic associations between polymorphic variants of MTHFR gene and the development of primary HD in adults.

Methods: Total 188 adults aged 52 [39; 63] years were examined. The control group consists of 81 healthy persons (67% of males and 33% of females), the primary HD group includes 107 patients, of which 72 (38% of males and 62% of females) with a tension HD and 35 (20% of males and 80% of females) with a migraine. Determination of single nucleotide variants (SNV) rs1801133 (c.677C>T; A222V) and rs 1801131 (c.1298A>C; E429A) of MTHFR gene was performed using RT-PCR.

Results: The MTHFR function promotes the homocysteine to methionine transformation. The A222V substitution in a homozygous state (TT) reduces the enzyme activity by 60%, which leads to an increase in homocysteine levels and reduces the pain threshold. Significant association between the carriage of variant T allele (OR 1.8; 95% CI 1.1-2–9; p =0.022) as well as CT genotype (OR 2.2; 95% CI 1.2-4.3; p = .024) of SNV rs1801133 and the development of tension HD was found. Variant T allele was also significantly associated with migraine (OR 2.0; 95% CI 1.1-3–ky allele and genotypes of rs1801131 and the primary HD was not shown.

Conclusion: Carriage of T allele of SNV rs1801133 increases the risk of tension HD and migraine development by 1.8 and 2.0 times, respectively.

Disclosure: No conflict of interest.

EPO-734

Indicators of Inflammation in Arachnoid of Patients with Atypical Trigeminal Neuralgia

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Background and aims: Paroxistic Trigeminal Neuralgia (TN) with continuous persistent pain or Atypical Trigeminal Neuralgia (ATN) it is a less common variation of the syndrome and represents greater difficulty in treatment. The role of inflammatory processes in the etiology of TN is still under debate. The aim of this study is to present the findings of inflammatory indicators in arachnoids from patients with ATN

Methods: From 49 patients with ATN between January of 2014 and December of 2018 who decided to undergo MVD as last option to treat their ATN, 22 samples of arachnoid tissue were in adequate conditions to be analyzed with immunohistochemical staining for the inflammation related markers CD20 and Epithelial Membrane Antigen (EMA), as well as hematoxylin-eosin staining.

Results: Hematoxylin-eosin stain revealed components of chronic arachnoiditis: fibrosis (n=28), dystrophic microcalcifications (n=11) and hyperplasia of neurothelial cells (n=7). CD20 was found in 6 (27.3%) while EMA was positive in all 22 samples (100%). Persistence and recurrence of pain was reported in 12 (24.5%) and 11 (22.4%) patients, respectively.

Conclusion: The findings described here are related to chronic inflammation. It will be analyzed whether these findings are more common in ATN compared to the classic form of TN which would support to propose an inflammatory process as the main cause in the etiology of ATN, since there is no neurovascular conflict and the symptoms are different from classical NT.

Disclosure: The authors have nothing to disclose.

EPO-735

Impact of erenumab in a Scandinavian chronic migraine population – an interim analysis of the IMPROVE phase IV trial

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Background and aims: Erenumab is a calcitonin gene-related peptide receptor antibody approved for migraine prevention in adults. Limited multicenter data has so far been published in the real-life setting. We here present interim data on headache-related quality of life after three and six months treatment with erenumab.
Methods: The IMPROVE study (Impact on Migraine-related Quality of Life in a non-controlled, real-world Population in the NoRdics treated with AimOVig®) is a one-year non-interventional phase IV trial, including 195 adult migraine patients on erenumab from 10 headache centers in Denmark, Sweden and Norway. The primary endpoint is change in HIT-6 at 12 months compared to baseline. The study is part of a larger umbrella protocol of studies with near-identical design, allowing for future data pooling. Here, a pre-planned interim analysis of IMPROVE was performed comparing multiple outcomes, including mean HIT-6 scores and mean monthly migraine days (MMD) at month three and six versus baseline.
Results: At time of interim analysis, 159 of 195 patients had entered the trial (baseline visit) at dose of either 70mg or 140mg (64.8% and 32.1% respectively, missing data for 3.1%). 98% (155/159) of patients fulfilled chronic migraine criteria (mean of 17.4 MMD). The mean HIT-6 score was reduced from 66.0 to 59.9 at three months and 59.5 at six months. The mean MMD was reduced by 41.4% at month six versus baseline.
Conclusion: The interim results thus far show an improvement of disease burden in chronic migraine patients treated with erenumab.
Disclosure: FMA, LE and ACP report lecturing and/or advisory board fee from Novartis, Teva, Eli Lilly and Lundbeck. US and AB are employees of Novartis.

EPO-736

Retrospective review of eight patients with HaNDL Syndrome

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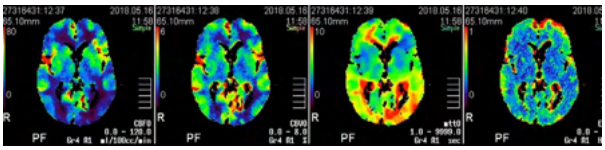
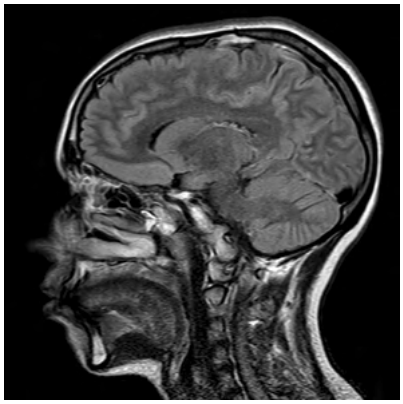
Background and aims: To describe the clinical characteristics of eight cases with Syndrome of transient headache and neurological deficits with cerebrospinal fluid lymphocytosis (HaNDL).
Methods: Retrospective review of patients diagnosed with HaNDL Syndrome in our center between January/2015-January/2020.
Results: Eight patients were included; six were male, with a median age of 40 years (range: 22–46). The most frequent symptoms were sensory (6 cases), aphasia (6), visual (4) and motor (2). 75% had at least one recurrence of neurological deficit, a median of three episodes (1–4). The median duration from the first episode to resolution of the last one was 7.5 days (1–20). No trigger was identified in any of them. six cases occurred in September/October. In CSF, the median opening pressure was 19.5 mmHg (8–50), proteins 85.5 mg/dL (45–140), leukocytes 161.5 /L (42–313), 92.5% (65–100) mononuclear. All (5/5) patients with an immunological study in CSF presented elevated IgM index and barrier dysfunction. four presented hypo-complementemia. SPECT was performed in six patients, showing hypoperfusion in four. In four cases, perfusion CT was done during the acute phase, with focal flow decrease in 3 of them. two patients presented foci of hyperintensity in grooves in the cranial MRI, disappearing in the followup MRI. 5 showed congruent focal EEG slowing, with subsequent normalization.



43 year-old man with intense headache followed by right hemiparesis and aphasia. Urgent CT perfusion showed a decline of cerebral blood flow with conservated cerebral blood volume in left occipitotemporal region.



22-year-old woman with intense headache, right hemiparesis and hypoesthesia and aphasia. MRI showed cerebrospinal fluid enhancement in occipital sulci.

Conclusion: There is a marked clinical variability among patients with HaNDL Syndrome. A better understanding of its characteristics is essential, given the absence of specific diagnostic tests.
Disclosure: Nothing to disclose.

Movement disorders 5

EPO-737

Non-motor symptoms in non-demented and non-depressed patients with Parkinson's disease

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Background and aims: Parkinson's disease (PD) is associated with spectrum of non-motor symptoms (NMS). NMS lead to a significantly reduced quality of life (QoL) and occur in all the patients with PD. The aim of our study was to analyze NMS in non-demented PD patients without depression.

Methods: We included 50 cognitively intact PD patients (30 men, mean PD duration 6.86y, LEDD 1,243.05mg). Scales and questionnaires for the assessment were used: Non-Motor Symptom Assessment Scale for PD (NMSS), Parkinson's Disease Questionnaire (PDQ-8), Geriatric Depression Scale (GDS), and Montreal Cognitive Assessment (MoCA). We excluded patients with MoCA < 26p and GDS >10p. Data were statistically analyzed (descriptive analysis, Spearman correlation coefficient).

Results: In our cohort, the most frequent NMS in domains of NSMS scale was: Sleep/fatigue, Urinary, Mood/Cognition, Sexual function, Miscellaneous. The correlation with QoL (PDQ-8) was in domains Cardiovascular including falls (r=0.435, p=0.002), Sleep/fatigue (r=0.515, p<0.001), Mood/Cognition (r=0.583, p<0.001), Urinary (r=0.283, p=0.046) and Sexual function (r=0.344, p=0.014).

Conclusion: NMS are very frequent in PD patients and have the most important impact on a reduced QoL. In our work we pointed out the most important NMS in non-demented and non-depressed PD patients. Targeted screening of NMS is therefore needed and it is very important to focus on managing these NMS.

Disclosure: Project was supported by the Grant of the Ministry of Health of the Slovak Republic 2018/32-LFUK-6.

EPO-738

Theory of mind in patients with spinocerebellar ataxia and idiopathic late onset cerebellar ataxia

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Background and aims: It has been well recognized that cerebellum has role not only in motor but also in cognitive and social cognitive functions. The aim of this study was to investigate the theory of mind (ToM) in patients with different cerebellar neurodegenerative disorders (CD).

Methods: In our research we directed our attention towards the three groups of subjects: 12 patients with spinocerebellar ataxia type 1 and six patients with spinocerebellar ataxia type 2 (SCA1+SCA2); 16 patients with idiopathic late onset cerebellar ataxia (ILOCA) and 54 matched healthy control (HC). All patients were evaluated clinically using the Scale for the Rating and Assessment of Ataxia (SARA). An appropriate battery of tests was used to assess global cognitive status as well as neuropsychological functions and mood. ToM studied using the Faux Pas Recognition Test and Reading the Mind in the Eyes Test - RMET.

Results: Our results were showed significant difference in average scores in Faux Pas Recognition Test (2=30.214; p=0.000) and RMET (2=43.380; p=0.000) between the three groups. We also found a significant difference in the average achievements on neuropsychological tests (except for Boston Naming Test, p=0.076) between these groups.

	SCA1+SCA2 (n=18)		ILOCA (n=16)		HC (n=54)	
	Mean (sd)	Range	Mean (sd)	Range	Mean (sd)	Range
THEORY OF MIND						
Faux Pas Recognition Test	63.9 (11.6)	37.0-80.0	78.8 (13.9)	46.3-93.3	87.1 (12.1)	64.8-100.0
Reading the Mind in the Eyes Test	52.8 (14.4)	25.0-72.2	64.4 (10.4)	38.9-77.8	82.2 (12.0)	52.8-100.0
NEUROPSYCHOLOGICAL SCREENING						
Global cognitive functioning						
MMSE[1]	27.2 (2.8)	19-30	27.8 (1.7)	25-30	29.8 (0.5)	28-30
ACE-R-Total[2]	82.6 (12.0)	56-99	89.9 (4.9)	80-98	96.1 (3.8)	86-100
Learning and episodic verbal memory[3]						
FCSRT-Total free recall	20.6 (6.8)	5-33	22.1 (4.9)	15-32	28.6 (6.6)	8-40
FCSRT-Delayed free recall	8.4 (2.7)	5-13	10.4 (2.5)	5-15	11.4 (2.7)	4-16
FCSRT-Recognition	14.4 (1.7)	12-16	15.5 (1.5)	10-16	15.9 (0.3)	14-16
ACE-R-Verbal Memory	21.7 (4.9)	6-26	23.3 (2.2)	19-26	25.4 (1.4)	18-26
Orientation and attention						
ACE-R-Orientation and attention	16.6 (1.8)	12-18	17.3 (0.9)	16-18	17.9 (0.2)	17-18
TMT-A	83.6 (36.6)	30-157	49.3 (17.0)	22-82	35.1 (16.1)	15-78
Digit-Span	7.7 (2.1)	4-11	8.3 (2.9)	4-13	10.9 (2.2)	5-15
Calculation						
Arithmetic-VITI[4]	9.1 (3.2)	3-14	11.3 (1.6)	9-14	13.6 (0.7)	11-14
Language						
ACE-R-Language	23.2 (3.2)	15-26	24.8 (0.8)	24-26	25.9 (0.4)	24-26
BNT-Total	50.3 (6.4)	40-58	53.3 (3.1)	45-57	54.0 (4.1)	40-59
Visuospatial processing						
JVOT[5]	17.2 (6.3)	8-25	21.3 (3.1)	16-25	24.3 (3.2)	13-30
ACE-R-Visuospatial skills	13.2 (3.1)	8-16	15.3 (1.0)	13-16	15.9 (0.4)	14-16
Executive functions						
Stroop test	91.61 (37.6)	45-154	97.3 (41.2)	36-180	58.9 (23.4)	10-100
DOT Total[6]	5.3 (1.9)	2-9	6.0 (1.3)	4-9	7.4 (2.2)	4-12
ACE-R-Phonemic Fluency	3.8 (1.6)	1-7	4.4 (1.5)	2-7	5.6 (0.9)	3-7
MOOD ASSESSMENT						
HDRS[7]	6.7 (4.1)	0-17	7.1 (3.9)	1-15	2.0 (2.9)	0-13
HARS[8]	9.6 (5.9)	0-17	7.3 (6.2)	0-17	2.4 (3.5)	0-19
AES[9]	9.5 (4.8)	2-22	7.5 (6.3)	0-23	1.9 (2.9)	0-15

[1] Mini Mental Screening Examination, [2] Addenbrooke's Cognitive Examination – Revised, [3] Free and cued selective reminding test, [4] Serbian adaptation of the Wechsler Adult Intelligence Scale – Revised, [5] Hooper Visual Organization Test, [6] Digit Ordering Test, [7] Hamilton Depression Rating Scale, [8] Hamilton Anxiety Rating Scale, [9] Apathy Evaluation Scale
Source: Author's calculation

Theory of Mind Tests, Neuropsychological Sreening, Mood Assessment – descpritive statistics

	Kruskal Vallis[a]		Groups	n=88	Mean Rank	Median
Faux Pas Recognition Test	Chi-Square	30.214	SCA1+SCA2	18	16.94	66.67
	df	2	ILOCA	16	41.06	82.60
	Sig.	0.000	HC	54	54.70	90.00
Reading of Mind in the Eyes Test	Chi-Square	43.380	SCA1+SCA2	18	16.78	55.56
	df	2	ILOCA	16	28.78	66.67
	Sig.	0.000	HC	54	58.40	83.33

a. Grouping Variable: Group (SCA1+SCA2, ILOCA, HC)
Source: Author's calculation

Differences in average scores on the Theory of Mind Tests

	Kruskal Vallis[a]		Groups	Mean Rank	Median
Global cognitive functioning					
MMSE	Chi-Square	39.371	SCA1+SCA2 (n=18)	24.92	27.5
	df	2	ILOCA (n=16)	26.50	27.5
	Sig.	0.000	HC (n=54)	56.36	30.0
ACE-R-Total	Chi-Square	35.547	SCA1+SCA2 (n=18)	19.42	85.5
	df	2	ILOCA (n=16)	30.41	89.0
	Sig.	0.000	HC (n=54)	57.04	97.0
Learning and episodic verbal memory					
FCSRT-Total free recall	Chi-Square	22.806	SCA1+SCA2 (n=18)	26.19	20.5
	df	2	ILOCA (n=16)	30.50	22.5
	Sig.	0.000	HC (n=54)	54.75	30.0
FCSRT-Delayed free recall	Chi-Square	14.072	SCA1+SCA2 (n=18)	26.11	8.5
	df	2	ILOCA (n=16)	41.00	10.0
	Sig.	0.001	HC (n=54)	51.67	12.0
FCSRT-Recognition	Chi-Square	24.312	SCA1+SCA2 (n=18)	27.22	14.5
	df	2	ILOCA (n=16)	44.47	16.0
	Sig.	0.000	HC (n=54)	50.27	16.0
ACE-R-Verbal Memory	Chi-Square	29.924	SCA1+SCA2 (n=18)	24.86	23.0
	df	2	ILOCA (n=16)	30.00	23.0
	Sig.	0.000	HC (n=54)	55.34	26.0
Orientation and attention					
ACE-R-Orientation and attention	Chi-Square	25.477	SCA1+SCA2 (n=18)	29.17	17.0
	df	2	ILOCA (n=16)	34.13	17.5
	Sig.	0.000	HC (n=54)	52.69	18.0
TMT-A	Chi-Square	31.953	SCA1+SCA2 (n=18)	70.94	74.0
	df	2	ILOCA (n=16)	53.25	42.5
	Sig.	0.000	HC (n=54)	33.09	32.0
Digit-Span	Chi-Square	23.710	SCA1+SCA2 (n=18)	24.69	8.0
	df	2	ILOCA (n=16)	32.06	8.0
	Sig.	0.000	HC (n=54)	54.79	11.0
Calculation					
Arithmetic-VITI	Chi-Square	47.185	SCA1+SCA2 (n=18)	17.53	9.0
	df	2	ILOCA (n=15)	27.33	11.0
	Sig.	0.000	HC (n=54)	57.45	14.0
Language					
ACE-R-Language	Chi-Square	41.799	SCA1+SCA2 (n=18)	25.00	25.0
	df	2	ILOCA (n=16)	27.19	25.0
	Sig.	0.000	HC (n=54)	56.13	26.0
BNT-Total	Chi-Square	5.146	SCA1+SCA2 (n=16)	32.44	52.0
	df	2	ILOCA (n=15)	38.60	54.0
	Sig.	0.076	HC (n=54)	47.35	55.0
Visuospatial processing					
HVOT	Chi-Square	24.912	SCA1+SCA2 (n=17)	22.68	17.0
	df	2	ILOCA (n=16)	31.94	21.5
	Sig.	0.000	HC (n=54)	54.29	25.0
ACE-R-Visuospatial skills	Chi-Square	25.126	SCA1+SCA2 (n=18)	26.11	14.0
	df	2	ILOCA (n=16)	39.88	16.0
	Sig.	0.000	HC (n=54)	52.00	16.0
Executive functions					
Stroop test	Chi-Square	18.400	SCA1+SCA2 (n=17)	57.76	90.0
	df	2	ILOCA (n=15)	59.30	98.0
	Sig.	0.000	HC (n=54)	34.62	53.0
DOT Total	Chi-Square	14.504	SCA1+SCA2 (n=18)	28.39	5.0
	df	2	ILOCA (n=16)	35.84	6.0
	Sig.	0.001	HC (n=54)	52.44	8.0
ACE-R-Phonemic Fluency	Chi-Square	23.748	SCA1+SCA2 (n=18)	24.81	4.0
	df	2	ILOCA (n=16)	32.75	4.0
	Sig.	0.000	HC (n=54)	54.55	6.0

a. Grouping Variable: Group (SCA1+SCA2, ILOCA, HC)
Source: Author's calculation

The differences in average scores on the neuropsychological tests

Conclusion: Our preliminary results show that social cognitive impairment in cerebellar neurodegenerative disorders is associated with ToM dysfunction and that impairment is present in different degenerative disorders of cerebellum. Patients with SCA1 and SCA2 exhibit a more pronounced impairment on ToM tests compared with ILOCA patients and this two groups exhibit different neuropsychological profiles.
Disclosure: No disclosure.

EPO-739

Data of P. Stradins Clinical University hospital Dystonia register: time from symptoms to diagnosis of cervical dystonia

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Background and aims: Cervical dystonia (CD) is characterized by excessive involuntary muscle contractions leading to abnormal postures of the neck and head. The diagnosis is based on clinical phenomenology. For almost 10 years patients with CD have been treated with Botulin neurotoxin (BoNT) injections at our BoNT outpatient's clinic.
Methods: The data was collected from P. Stradins Clinical University hospital BoNT clinic local register. Overall 147 patients data who visited our clinic from January 2018 till December 2020 were analyzed.
Results: Majority 78% (114) of the CD patients were women. Mean age was 51,1 (SD±13 years) with youngest patient being 21 and the oldest patient 82 years old (figure 1). Mean time from first symptoms till the diagnosis were 4,38 years (SD±4 years). In majority of patients (64%) diagnosis of CD was established in less than four years – 54 patients were diagnosed in a year or less, 40 patients received diagnosis in 2–4 years after the manifestation of first symptoms. In minority of patients 53 (36%) diagnosis was established in more than five years from the symptom presentation. Longest period of time from symptoms till diagnosis was 23 years.

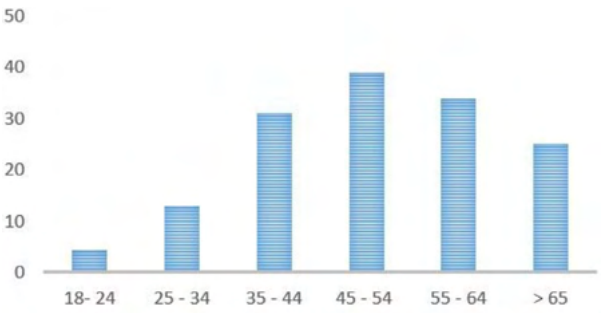

Figure 1 Prevalence of cervical dystonia in different age groups

Conclusion: Unfortunately, the accurate diagnosis of CD is still delayed in Latvia. For some patients it takes more than five years till diagnosis is established. More educational activities should be carried out to improve awareness and recognition about CD amongst general neurologists and general practitioners.
Disclosure: Nothing to disclose.

EPO-740

Non-motor symptoms in Parkinson's disease patients in Kyrgyzstan

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Background and aims: Non-motor symptoms (NMS) have a great impact on lives of patients with Parkinson's Disease (PD). There was no study previously conducted on prevalence of NMS in Kyrgyzstan. Aim of this study was to determine the frequency of NMS in patients with PD.

Methods: One-month survey was conducted at movement disorders service, working one day/week in the outpatient clinic of the Clinical Hospital of the AD PGA, Bishkek, Kyrgyzstan. 28 PD patients filled NMS questionnaire (NMSQ). All respondents were fluent in Russian language. PD diagnosis was based on UK Brain Bank Clinic Diagnostic Criteria.

Results: 55% of all visited PD patients filled NMSQ. The mean age was 63.04±11.22 years, where 46.4% males and 53.6% females took part in survey. The data on stage and type of disease is indicated in table 1. 8.3% of patients had Hoehn-Yahr stage one, 45.8% – Hoehn-Yahr stage 2, combined into group – mild disease. 37.5% and 8.3% – Hoehn-Yahr stages 3 and 4 – severe disease. Complete data is provided in figure 1.The most common NMS was insomnia – 82.1%. Bowel incontinence was the least responded symptom – 7.1%. 78.6% of patients had low mood, anxiety – 71.4%. Memory problems were indicated by 57.1%, whereas concentration problems – by 39.3%. Complete data on NMS is indicated in figure 2.

Table 1. Demographic data

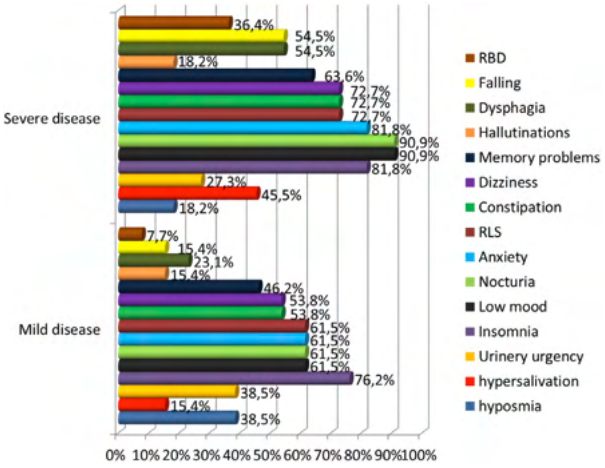

Figure 1. Comparison of frequency of NMS in mild and severe diseases

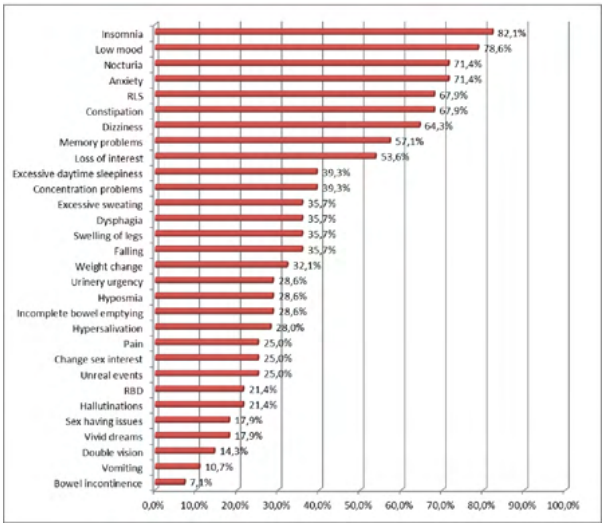

Figure 2. Non-motor symptoms among patients with PD

Conclusion: The NMS are quite prevalent in PD patients from Kyrgyzstan. Comparing to studies from other countries, patients from Kyrgyzstan have higher frequency of depression, anxiety, insomnia, and RLS. The matter requires further detailed evaluation and study.

Disclosure: The authors declare no sources of support or conflict of interest.

EPO-741

Bilateral upper limbs pseudoathetosis in cervical spine myelitis

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Background and aims: Pseudoathetotic movements can occur in patients with loss of proprioception caused by lesions at various parts of the sensory pathways, including the spinal cord.
Methods: We report the observation of striking pseudoathetotic movements, with an impulsive behavior to manipulate objects with both hands, in man with cervical spine myelitis.
Results: A 77-year-old man was admitted for an acute onset of difficulties in performing voluntary movements with his hands, especially the left one. Symptoms appeared after use of Bactefort for two days (an antiparasitar combination of plant ingredients). Strength was normal in upper and lower limbs. Plantar reflexes were flexor on both sides. Vibration and positional joint sensation were reduced, but temperature and pain sensation were normal. There were involuntary movements of both hands (fingers and wrist) induced by movement. Motor abilities were severely impaired. Serum analysis and tumor markers were normal. Cranial MRI showed cortical atrophy. Spinal cord MRI scan showed a predominantly posterior hyperintense lesion in the cervical spinal cord, extending from C2 to C3, compatible with myelitis. The patient was treated with corticosteroids and Acyclovir. The evolution was favorable with the improvement of the neurological symptoms and and a minimal reduction of lesion on spinal cord MRI.
Conclusion: Biilateral upper limbs pseudoathetosis is a rare movement disorders that may have as etiology cervical spine myelitis.
Disclosure: Nothing to disclose.

EPO-742

Essential Tremor Actually is not a Benign Movement Disorder; Progression to Dementia

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Background and aims: Essential tremor is one of the most common movement disorders characterized by kinetic tremor. Until recently, it was considered to be mono-symptomatic. However, it has been reported for the last two decades that motor and non-motor findings other than kinetic tremor may accompany the disease. In this report, cases presenting with isolated kinetic tremor and developing dementia during their follow-up will be evaluated together with their clinical features.
Methods: The records of the cases evaluated in the dementia polyclinics were retrospectively analyzed. The demographic and clinical characteristics of cases with isolated kinetic tremor consistent with essential tremor were noted.
Results: There were eight patients diagnosed with dementia in the follow-up after essential tremor. The mean of onset ages of kinetic tremor was 65.75 (±7.5). The mean of the interval from the onset of tremor to the other neurologic findings was calculated 8.86 (±6.58) years. Parkinsonian findings were also observed in the follow-up of six patients. In detailed neurocognitive evaluation, depression was found in half of the patients. Also, in the half of the patients dysfunction in attention, expressive behaviors and visiospatial skills were prominent.
Conclusion: Essential tremor, which is considered to be part of a spectrum of disorders, has also a spectrum of symptoms within itself. This report also supported that other neurodegenerative diseases may accompany essential tremor. In addition, in the half of the cases described here, the clinical picture is compatible with dementia with Lewy bodies. Publications on this association in the literature are very limited.
Disclosure: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version. Additionally, there are no conflicts of interest in connection with this paper.

EPO-743

Opsoclonus-myoclonus syndrome (OMS) during pregnancy – a clinical case

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Background and aims: Opsoclonus is manifested by irregular saccadic eye movements that occur periodically or constantly present, and do not decrease in the dark and with eyes closed. The clinical picture is characterized by the staged development of symptoms.

Methods: A 41-year-old female patient was admitted at the 37th week of pregnancy at the antenatal department with complaints of imbalance in sitting and standing, inability to walk due to pronounced shakiness, visual impairment in the form of a sensation of "trembling" of objects when looking directly ahead, twitching of the head, trunk and limbs, episodic diffuse headache. A history of rotavirus infection within a week. During the study medical history, somatic and neurological status, laboratory, neuroimaging and electrophysiological data were evaluated. Antineuronal antibodies were also screened, antibodies (IgM) for gangliosides were tested, and oncological searches were negative.

Results: Neurological status: spontaneous non-rhythmic saccadic movements of the eyeballs in the horizontal plane, myoclonus in many muscle groups, tremor of the head, and body, rough right-sided pyramidal and cerebellar symptoms were noted. Meningeal symptoms were negative. At the 40th week of pregnancy, the patient was delivered per vies naturalis, without complications. After Methylprednisolone and neuroprotective therapy, the patient was discharged on day 56 of illness.

Conclusion: A feature of this case is that the autoimmune process started during pregnancy (most likely triggered by a previous viral infection), when physiological immunosuppression. As a confirmation of the autoimmune genesis, a positive response to immunosuppressive therapy can be considered.

Disclosure: No disclosure.

EPO-744

Opicapone OCEAN study in Parkinson's: design of a randomized double-blind placebo-controlled trial

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Background and aims: Opicapone (OPC) proved to be effective in the treatment of end-of-dose motor fluctuations in Parkinson's Disease (PD) patients [1,2]. End-of-dose motor fluctuations and associated pain are commonly observed in PD patients on L-dopa/DOPA decarboxylase inhibitors (DDCI). They have a detrimental impact on the quality-of-life [3] and are in part mediated via dopaminergic pathways. [4]. Therefore, an a-priori presumption was made that OPC will overcome end-of-dose fluctuation related pain and consequently improve patients' well-being.

Methods: Patients (30 years old) with idiopathic PD, treated with three to eight daily oral doses of L-dopa/DDCI and with 'wearing-off' (end-of-dose deterioration) phenomenology, and experiencing PD associated pain will be randomised (1:1) to OPC 50mg once-daily or placebo during a 24-week evaluation-period (Figure 1). To detect a minimum clinically relevant magnitude of effect between arms, 70 subjects per group is necessary.

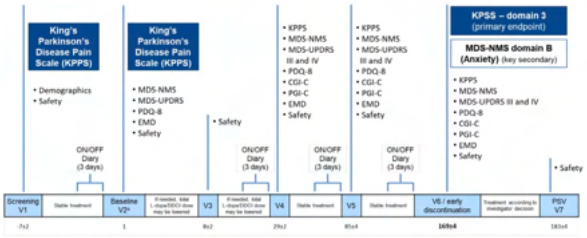

Figure 1. Overall OCEAN study design.
* V2 is divided in V2a and V2b. If ON/OFF diary entries are non-compliant at V2a, the patient will be re-trained on correct use of the diary and visit V2b will be postponed for 3-4 days. If diary completion is satisfactory at V2a, V2b is performed immediately at the same day.
MDS: Movement Disorder Society. UPDRS: Unified Parkinson's Disease Rating Scale. NMS: Non-Motor Symptoms. EMD: Early Morning Dystonia. PDQ-8: Parkinson's Disease Questionnaire 8-item. PGI-C: Patient Global Impression of Change. CGI-C: Clinical Global Impression of Change. PSV: Post-Study Visit.

Results: The primary endpoint is change from baseline in Domain 3 (fluctuation-related pain) of King's-Parkinson's-Disease-Pain-Scale (KPPS). Secondary endpoints include tolerability, functional motor and non-motor assessments (KPSS, MDS-NMS, PDQ-8, Hauser's home diary), and Global Impression of Change (CGI-C, PGI-C). Study sites are in Germany, Italy, Portugal, Spain and UK. First-patient-in is expected for 2021 and Last-patient-out to late 2022. Timelines might be impacted by COVID-19 pandemic situation.

Conclusion: This study will further evaluate the impact of 50mg opicapone once daily as adjunctive therapy to L-dopa/DDCI on fluctuation-associated pain.

Disclosure: 1.Ferreira et al., Lancet Neurol. 2016;15(2):154-165; 2.Lees et al., JAMA Neurol. 2017;74(2):197-206; 3.Gökçal et al., Noro Psikiyatr Ars. 2017;54(2):143-148; 4.Antonini et al., Eur J Neurol. 2018;25(7):917-e69

EPO-745

Influence of demographic features in Opicapone effectiveness in Parkinson's patients: the real-world OPTIPARK study

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Background and aims: Opicapone (OPC) proved to be effective in treating end-of-dose motor fluctuations (MF) in Parkinson's Disease (PD) patients [1,2]. The OPTIPARK study evaluated OPC 50mg in a heterogeneous population of patients treated in real-world conditions [3].

Methods: OPTIPARK was a prospective, open-label, single-arm trial conducted in Germany and the UK. Patients with MF received OPC 50mg in addition to current antiparkinsonian treatment. Primary efficacy three-month endpoint was Clinician's-Global-Impression-of-Change (CGI-C). Secondary efficacy endpoints included Patient's-CGI-C (PGI-C), 8-item PD Questionnaire (PDQ-8), Unified PD Rating (UPDRS) and Non-Motor Symptoms (NMSS) scales. Safety assessments included evaluation of treatment-emergent adverse-events (TEAEs). This post-hoc analysis evaluated the influence of demographic characteristics (i.e., age and gender) in patients who completed the study for each outcome.

Results: 393 (82.4%) patients completed the three-month endpoint (completers-set, Table 1). Of these, younger (<67.2 years-old) and female patients experienced greater very-much/much improvement on CGI-C and PGI-C, when compared, respectively, to older and male patients (Table 2). Except for UPDRS-II, younger and male patients reported greater improvements on UPDRS-III, PDQ-8 and NMSS, when compared to older and female patients (Table 3). Lower incidence of TEAEs considered at least possibly related to OPC were reported for younger and male patients, when compared to older and female patients (Table 3).

Table 1. Baseline characteristics (Completer-Set)

Category	< 67.2* years old	≥ 67.2* years old	Male	Female
	N=179	N=214	N=257	N=135
Age, mean (SD)	58.9 (5.7)	74.1 (4.4)	66.9 (8.9)	67.7 (9.2)
Male, n (%)	119 (66.5)	138 (64.5)	-	-
PD duration, mean (SD) years	7.8 (4.2)	8.9 (4.9)	8.5 (4.6)	8.1 (4.7)
Onset of MF, mean (SD) years	2.3 (2.7)	2.5 (3.2)	2.6 (3.1)	2.1 (2.8)
Ldopa amount, mean (SD) mg	538 (244.5)	574 (247.2)	583.1 (248.3)	513.4 (237.2)

*mean age at baseline; SD, standard deviation; PD, Parkinson's Disease; MF, motor fluctuations

Table 2. CGI-C and PGI-C results after 3 months (Completer-Set)

Category	< 67.2* years old	≥ 67.2* years old	Male	Female
	N=179	N=214	N=257	N=135
	n (%)	n (%)	n (%)	n (%)
CGI-C				
Not assessed	-	-	-	-
Very much improved	21 (11.7)	9 (4.2)	17 (6.6)	13 (9.6)
Much improved	81 (45.3)	86 (40.2)	105 (40.9)	61 (45.2)
Minimally improved	54 (30.2)	69 (32.2)	88 (34.2)	35 (25.9)
No change	16 (8.9)	40 (18.7)	35 (13.6)	21 (15.6)
Minimally worse	6 (3.4)	7 (3.3)	10 (3.9)	3 (2.2)
Much worse	-	3 (1.4)	2 (0.8)	1 (0.7)
Very much worse	1 (0.6)	-	-	1 (0.7)
PGI-C				
Not assessed	-	-	-	-
Very much improved	18 (10.1)	12 (5.6)	19 (7.4)	11 (8.1)
Much improved	84 (46.9)	75 (35.0)	99 (38.5)	59 (43.7)
Minimally improved	52 (29.1)	61 (28.5)	77 (30.0)	36 (26.7)
No change	14 (7.8)	44 (20.6)	40 (15.6)	18 (13.3)
Minimally worse	9 (5.0)	16 (7.5)	18 (7.0)	7 (5.2)
Much worse	1 (0.6)	5 (2.3)	3 (1.2)	3 (2.2)
Very much worse	1 (0.6)	1 (0.5)	1 (0.4)	1 (0.7)

*mean age at baseline; CGI-C, Clinician's Global Impression of Change; PGI-C, Patient's Global Impression of Change

Table 3. Secondary, after 3 months, and safety outcomes (Completer-Set)

Category	< 67.2* years old	≥ 67.2* years old	Male	Female
	N=179	N=214	N=257	N=135
	mean (SD)	mean (SD)	mean (SD)	mean (SD)
UPDRS II (at ON stage)	-1.5 (3.76)	-1.7 (3.72)	-1.5 (3.80)	-1.8 (3.57)
p-value	*<.0001*	*<.0001*	*<.0001*	*<.0001*
UPDRS III	-5.0 (8.40)	-4.4 (7.81)	-4.7 (8.25)	-4.4 (7.79)
p-value	*<.0001*	*<.0001*	*<.0001*	*<.0001*
PDQ-8	-3.99 (13.18)	-2.98 (12.54)	-3.78 (13.16)	-2.80 (12.26)
p-value	*0.0001*	*0.0006*	*<.0001*	*0.0089*
NMSS	-8.7 (20.09)	-5.2 (19.36)	-7.6 (20.81)	-5.4 (17.57)
p-value	*<.0001*	*0.0001*	*<.0001*	*0.0005*
Any TEAE, **n (%)**	128 (71.5)	153 (71.5)	179 (69.65)	101 (74.5)
At least possibly related* TEAEs, **n (%)**	69 (38.5)	85 (64.4)	95 (37.0)	58 (43.0)

*mean age at baseline; SD, standard deviation; UPDRS, Unified Parkinson's Disease Rating Scale; PDQ-8, 8-item Parkinson's Disease Questionnaire; NMSS, Non-Motor Symptoms Scale; p-values obtained through Student's t-test for the change from baseline; *relationship to study medication reported as 'possible', 'probable', 'definite' or missing; TEAE, treatment-emergent adverse event (with onset or worsening after first opicapone intake until study termination, either regularly or prematurely)

Conclusion: These findings indicate that younger PD patients with MF may have an added benefit from using OPC 50 mg as adjunctive therapy to levodopa.

Disclosure: 1.Ferreira et al., Lancet Neurology 2016;15(2):154-165; 2.Lees et al., JAMA Neurol. 2017;74(2):197-206; 3.Reichmann et al., Transl Neurodegener. 2020;9(1):9

EPO-746

Influence of disease duration in the Opicapone effectiveness in Parkinson's patients: real-world OPTIPARK study

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Background and aims: Opicapone (OPC) proved to be effective in treating end-of-dose motor fluctuations (MF) in Parkinson's Disease (PD) patients [1,2]. The OPTIPARK study evaluated OPC 50mg in a heterogeneous population of patients treated in real-world conditions [3].

Methods: OPTIPARK was a prospective, open-label, single-arm trial conducted in Germany and the UK. Patients with MF received OPC 50mg in addition to current antiparkinsonian treatment. Primary efficacy three-month endpoint was Clinician's-Global-Impression-of-Change (CGI-C). Secondary efficacy endpoints included Patient's-CGI-C (PGI-C), 8-item PD-Questionnaire (PDQ-8), Unified PD Rating Scale (UPDRS) and Non-Motor Symptoms Scale (NMSS). Safety assessments included evaluation of treatment-emergent adverse events (TEAEs). This post-hoc analysis evaluated the influence of disease duration at baseline in patients who completed the study for each outcome.

Results: 393 (82.4%) patients completed the three-month endpoint (completers-set, Table 1). Of these, patients with 'less-disease' duration experienced greater very-much/much improvement on CGI-C and PGI-C, when compared to patients with 'longer-disease' duration (Table 2). Except for UPDRS, patients with 'less-disease' duration experienced greater improvements on quality-of-life (PDQ-8) and non-motor symptoms (NMSS), when compared to patients with 'longer-disease' duration (Table 3). Lower incidence trend of TEAEs considered at least possibly related to OPC were also observed for patients with 'less-disease' duration (Table 3).

Table 1. Baseline characteristics (Completer-Set)

Category	PD duration at baseline					
	< 6.5years	≥ 6.5years	< 8.4years*	≥ 8.4years*	< 10.5years	≥ 10.5years
	N=179	N=214	N=204	N=189	N=293	N=100
Age, mean (SD)	65.8 (9.7)	68.1 (8.5)	66.1 (9.5)	68.5 (8.3)	66.7 (9.4)	68.5 (8.1)
Male, n (%)	100 (55.9)	157 (73.4)	135 (66.2)	122 (64.6)	184 (62.8)	73 (73.0)
PD duration, mean (SD) years	4.2 (1.5)	11.3 (3.8)	5.0 (1.9)	12.5 (3.5)	6.0 (2.5)	14.4 (3.2)
Onset of MF, mean (SD) years	1.1 (1.1)	3.3 (3.5)	1.3 (1.6)	3.7 (3.7)	1.6 (1.8)	4.4 (4.2)
Ldopa amount, mean (SD) mg	506 (231)	595 (251)	524 (240)	599 (248)	536 (240)	613 (255)

*mean PD duration at baseline; SD, standard deviation; PD, Parkinson's Disease; MF, motor fluctuations

Table 2. CGI-C and PGI-C results after 3 months (Completer-Set)

Category	PD duration at baseline					
	< 6.5years	≥ 6.5years	< 8.4years*	≥ 8.4years*	< 10.5years	≥ 10.5years
	N=179 n (%)	N=214 n (%)	N=204 n (%)	N=189 n (%)	N=293 n (%)	N=100 n (%)
CGI-C						
Not assessed	-	-	-	-	-	-
Very much improved	17 (9.5)	13 (6.1)	18 (8.8)	12 (6.3)	22 (7.5)	8 (8.0)
Much improved	82 (45.8)	85 (39.7)	92 (45.1)	75 (39.7)	129 (44.0)	38 (38.0)
Minimally improved	47 (26.3)	76 (35.5)	58 (28.4)	65 (34.4)	89 (30.4)	34 (34.0)
No change	29 (16.2)	27 (12.6)	30 (14.7)	26 (13.8)	44 (15.0)	12 (12.0)
Minimally worse	3 (1.7)	10 (4.7)	5 (2.5)	8 (4.2)	7 (2.4)	6 (6.0)
Much worse	-	3 (1.4)	-	3 (1.6)	1 (0.3)	2 (2.0)
Very much worse	1 (0.6)	-	1 (0.5)	-	1 (0.3)	-
PGI-C						
Not assessed	-	-	-	-	-	-
Very much improved	15 (8.4)	15 (7.0)	15 (7.4)	15 (7.9)	24 (8.2)	6 (6.0)
Much improved	77 (43.0)	82 (38.3)	89 (43.6)	70 (37.0)	121 (41.3)	38 (38.0)
Minimally improved	45 (25.1)	68 (31.8)	52 (25.5)	61 (32.3)	80 (27.3)	33 (33.0)
No change	28 (15.6)	30 (14.0)	33 (16.2)	25 (13.2)	47 (16.0)	11 (11.0)
Minimally worse	10 (5.6)	15 (7.0)	11 (5.4)	14 (7.4)	16 (5.5)	9 (9.0)
Much worse	2 (1.1)	4 (1.9)	2 (1.0)	4 (2.1)	3 (1.0)	3 (3.0)
Very much worse	2 (1.1)	-	2 (1.0)	-	2 (0.7)	-

*mean PD duration at baseline; CGI-C, Clinician's Global Impression of Change; PGI-C, Patient's Global Impression of Change

Table 3. Secondary, after 3 months, and safety outcomes (Completer-Set)

Category	PD duration at baseline					
	< 6.5years	≥ 6.5years	< 8.4years*	≥ 8.4years*	< 10.5years	≥ 10.5years
	N=179 mean (SD)	N=214 mean (SD)	N=204 mean (SD)	N=189 mean (SD)	N=293 mean (SD)	N=100 mean (SD)
UPDRS II (at ON stage)	-1.6 (3.6)	-1.6 (3.8)	-1.5 (3.5)	-1.7 (3.9)	-1.6 (3.5)	-1.6 (4.3)
p-value	*<.0001*	*<.0001*	*<.0001*	*<.0001*	*<.0001*	*0.0003*
UPDRS III	-4.1 (6.9)	-5.1 (9.0)	-4.4 (6.9)	-4.9 (9.2)	-4.3 (7.7)	-5.5 (9.1)
p-value	*<.0001*	*<.0001*	*<.0001*	*<.0001*	*<.0001*	*<.0001*
PDQ-8	-4.2 (12.7)	-2.8 (12.9)	-4.6 (12.8)	-2.2 (12.8)	-3.7 (12.9)	-2.7 (12.7)
p-value	*<.0001*	*0.0016*	*<.0001*	*0.0174*	*<.0001*	*0.0367*
NMSS	-8.9 (20.9)	-5.1 (18.6)	-8.8 (20.7)	-4.7 (18.5)	-7.7 (19.8)	-4.2 (19.3)
p-value	*<.0001*	*0.0001*	*<.0001*	*0.0006*	*<.0001*	*0.0305*
Any TEAE, n (%)	122 (68.2)	159 (74.3)	137 (67.2)	144 (76.2)	207 (70.6)	74 (74.0)
At least possibly related[a] TEAEs, n (%)	65 (36.3)	89 (41.6)	75 (36.8)	79 (41.8)	118 (40.3)	36 (36.0)

*mean PD duration at baseline; SD, standard deviation; UPDRS, Unified Parkinson's Disease Rating Scale; PDQ-8, 8-item Parkinson's Disease Questionnaire; NMSS, Non-Motor Symptoms Scale; p-values obtained through Student's t-test for the change from baseline; [a]relationship to study medication reported as 'possible', 'probable', 'definite' or missing; TEAE, treatment-emergent adverse event (with onset or worsening after first opicapone intake until study termination, either regularly or prematurely)

Conclusion: Overall, these findings indicate that patients with less years of PD duration (representative of recent fluctuators) may have an added benefit from using OPC 50 mg as adjunctive therapy to levodopa.

Disclosure: 1.Ferreira et al., Lancet Neurology 2016;15(2):154-165; 2.Lees et al., JAMA Neurol. 2017;74(2):197-206; 3.Reichmann et al., Transl Neurodegener. 2020;9(1):9

EPO-747

Effectiveness of Opicapone in Parkinson's according to baseline use of dopamine agonists: the real-world OPTIPARK study

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Background and aims: Opicapone (OPC) proved to be effective in treating end-of-dose motor fluctuations (MF) in Parkinson's disease (PD) patients [1,2]. The OPTIPARK study evaluated OPC 50mg in a heterogeneous population of patients treated in real-world conditions [3].

Methods: OPTIPARK was a prospective, open-label, single-arm trial conducted in Germany and the UK. Patients with MF received OPC 50mg in addition to current antiparkinsonian treatment. Primary efficacy three-month endpoint was Clinician's-Global-Impression-of-Change (CGI-C). Secondary efficacy endpoints included Patient's-CGI-C (PGI-C), 8-item PD-Questionnaire (PDQ-8), Unified PD Rating Scale (UPDRS) and Non-Motor Symptoms Scale (NMSS). Safety assessments included evaluation of treatment-emergent adverse events (TEAEs). This post-hoc analysis evaluated, for each outcome, the influence according to baseline use of dopamine-agonists (DA) in patients who completed the study.

Results: 393 (82.4%) patients completed the three-month endpoint (completers-set, Table 1). Of these, patients using DA at baseline experienced greater improvements on CGI-C and PGI-C, when compared to patients NOT using DA at baseline (Table 2). Except for UPDRS-II, patients using DA at baseline experienced greater improvements on UPDRS-III, quality-of-life (PDQ-8) and non-motor symptoms (NMSS), when compared to patients NOT using DA at baseline (Table 3). Lower incidence of TEAEs considered at least possibly related to OPC were also reported for patients using DA at baseline (Table 3).

Table 1. Baseline characteristics (Completer-Set)

Category	Used DA at Baseline N=279	Not Used DA at Baseline N=114
Age, mean (SD)	66.0 (8.9)	70.0 (8.9)
Male, n (%)	181 (64.9)	76 (66.7)
PD duration, mean (SD) years	9.0 (4.7)	6.8 (4.3)
Onset of MF, mean (SD) years	2.6 (3.1)	2.0 (2.7)
L-dopa amount, mean (SD) mg	538 (242)	606 (254)

SD, standard deviation; PD, Parkinson's disease; MF, motor fluctuations; OMF, onset of MF

Table 2. CGI-C and PGI-C results after 3 months (Completer-Set)

Category	Used DA at Baseline N=279 n (%)	Not Used DA at Baseline N=114 n (%)
CGI-C		
Not assessed	-	-
Very much improved	23 (8.2)	7 (6.1)
Much improved	123 (44.1)	44 (38.6)
Minimally improved	88 (31.5)	35 (30.7)
No change	32 (11.5)	24 (21.1)
Minimally worse	9 (3.2)	4 (3.5)
Much worse	3 (1.1)	-
Very much worse	1 (0.4)	-
PGI-C		
Not assessed	-	-
Very much improved	21 (7.5)	9 (7.9)
Much improved	121 (43.4)	38 (33.3)
Minimally improved	81 (29.0)	32 (28.1)
No change	32 (11.5)	26 (22.8)
Minimally worse	20 (7.2)	5 (4.4)
Much worse	3 (1.1)	3 (2.6)
Very much worse	1 (0.4)	1 (0.9)

OMF, onset of motor fluctuations; CGI-C, Clinician's Global Impression of Change; PGI-C, Patient's Global Impression of Change

Table 3. Secondary, after 3 months, and safety outcomes (Completer-Set)

Category	Used DA at Baseline N=279	Not Used DA at Baseline N=114
UPDRS II (at ON stage), mean (SD)	-1.5 (3.6)	-1.9 (4.1)
p-value	*<.0001*	*<.0001*
UPDRS III, mean (SD)	-4.8 (8.4)	-4.3 (7.3)
p-value	*<.0001*	*<.0001*
PDQ-8, mean (SD)	-3.6 (12.4)	-3.0 (13.8)
p-value	*<.0001*	*0.0217*
NMSS, mean (SD)	-8.0 (19.1)	-3.8 (21.0)
p-value	*<.0001*	*0.0557*
Any TEAE, n (%)	198 (71.0)	83 (72.8)
At least possibly related[a] TEAEs, n (%)	106 (38.0)	48 (42.1)

OMF, onset of motor fluctuations; SD, standard deviation; UPDRS, Unified Parkinson's Disease Rating Scale; PDQ-8, 8-item Parkinson's Disease Questionnaire; NMSS, Non-Motor Symptoms Scale; p-values obtained through Student's t-test for the change from baseline; [a]relationship to study medication reported as 'possible', 'probable', 'definite' or missing; TEAE, treatment-emergent adverse event (with onset or worsening after first opicapone intake until study termination, either regularly or prematurely)

Conclusion: Overall, these findings indicate that patients may similarly benefit of using or not DA and OPC 50 mg as adjunctive therapy to levodopa.

Disclosure: 1.Ferreira et al., Lancet Neurology 2016;15(2):154-165; 2.Lees et al., JAMA Neurol. 2017;74(2):197-206; 3.Reichmann et al., Transl Neurodegener. 2020;9(1):9

EPO-748

Opicapone effect at different levodopa regimens up to 600 mg/d threshold in Parkinson's patients and motor fluctuations

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Background and aims: Opicapone (OPC) was effective for end-of-dose motor fluctuations in PD patients in two large multinational trials [1,2].
Methods: Efficacy data were combined for the placebo (PLC) and OPC-50mg groups [1,2]. Primary efficacy endpoint was change from baseline in OFF-time based on patient diaries. Subgroup analyses were performed to evaluate the OPC-50mg effect at different levodopa regimens up to a threshold of 600 mg/day (300–400, 400–500 and 500–600 mg/day).
Results: 239 patients were included in the Full-Analysis-Set (PLC, n=118; OPC-50mg, n=121). Mean OFF-time reduction when OPC-50mg was added to any levodopa regimen was at least double that of PLC: mean (95% confidence interval) changes from baseline in absolute OFF-time for OPC-50mg versus PLC were -102.2 (-138.1, -66.3) versus -53.4 (-89.6, -17.3) min for patients treated with levodopa 300–400 mg/day, -110.0 (-146.7, -73.3) versus -37.2 (-77.7, 3.3) min for patients treated with levodopa 400–500mg/day, and -117.6 (-152.6, -82.6) versus -23.1 (-67.8, 21.6) min for patients treated with levodopa 500–600mg/day. It was notable that, with increasing levodopa dose regimens, there was a trend towards decreasing magnitude of effect in the PLC group, compared with a trend towards a slight increase in magnitude of effect in the OPC-50mg group.
Conclusion: OPC-50mg showed a similar magnitude of effect between different low levodopa dose regimens, with at least a two-fold greater OFF-time reduction than placebo.
Disclosure: 1 Ferreira et al., Lancet Neurol. 2016;15(2):154-165; 2.Lees et al., JAMA Neurol. 2017;74(2):197-206

EPO-749

Heart rate variability: a possible biomarker of dysautonomia in Parkinson's disease?

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Background and aims: Dysautonomic symptoms are common in later stages of Parkinson's disease (PD), are also present at the onset of the disease. Heart rate variability (HRV), defined as beat-to-beat changes in normal R-R intervals, represents a non-invasive measurement of cardiac autonomic system. In healthy subjects, HRV had a linear decrease with increasing age. We evaluated changes in time-domain parameters (SDNN, rMSSD, pNN50, I-SDANN, I-SDNN) of HRV in a sample of PD patients during a five years follow-up study.
Methods: We determined HRV of 15 PD patients by ambulatory 24-hour electrocardiogram-holter (ECG-holter), including night and day, at baseline and at a five years follow-up. All patients were evaluated by Hoehn and Yahr staging (H&Y), Unied Parkinson's disease rating scale (UPDRS) and Neuropsychiatric inventory (NPI). Autonomic disfunction was graded by SCOPA-AUT scale, and Levodopa Equivalent Daily Dose (LEDD) were also calculated.
Results: After five years follow-up, mean scores of UPDRS (section three), SCOPA-AUT and NPI, were significantly greater compared to baseline. In our study, at second ECG-holter evaluation, no significant difference between SDNN, rMSSD, pNN50, I-SDANN, I-SDNN compared to first evaluation was observed. However, as supplementary finding, the difference between mean scores of SDNN-N and SDNN-D A at baseline (23.2) was significantly (p=0.04) greater than that observed after five years (1.2).
Conclusion: Though hearth rate variability could not be a good marker of progression of dysautonomia, in our study, it showed to be helpful to interpret the occurrence of nocturnal symptoms (i.e. nicturia), resulting from a change of autonomic control, especially during night period.
Disclosure: Nothing to disclose.

EPO-750

The first case of a child with a dopamine transporter deficiency associated with SLC6A3 in Russia

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Background and aims: We report the first case of a child with a dopamine transporter deficiency associated with SLC6A3 in Russia.
Methods: A study of an 1.5-year-old girl, included anamnesis, physical neurological examination, and analysis of instrumental and genetic tests.
Results: The child from a closely related marriage. The disease debuted with torticollis at the age of two months. There were the regurgitation, fountain vomiting and muscle spasticity. Hyperkinesis such as choreoathetosis, oromandibular dystonia, axial muscle dystonia, dystonic tremor, and development delay were identified at age of four months. Neurological examination revealed a hypomimic face, violent protrusion of the tongue. The child was lethargic, often throws her head back. The girl cannot sit, roll over, make sounds, swallow the saliva. Massage could induce an arousal attack with a dystonic status. MRI of the brain: atrophic changes in the brain, hypoplasia of the corpus callosum. In May 2020, the girl had been ill with COVID-19, her condition worsened, hyperkinesis became more pronounced, expressed anxiety, and rare dystonic statuses appeared. DNA panel: detected in exon 10 of the SLC6A3 gene nucleotide substitution chr5-1409937-C-N, NM_001044.4: c.1297G> A, p. (Gly433Arg) in a homozygous state.
Conclusion: Dopamine transporter deficiency syndrome associated with SLC6A3 (DTDS) is a very rare complex movement disorder with a continuum that ranges from classic DTDS with early onset in the first six months to atypical DTDS with later onset in childhood, adolescence. According to the results of the examination, the patient has infant parkinsonism-dystonia type 1, homozygous gene carriage.
Disclosure: Nothing to disclose.

MS and related disorders 4

EPO-751

Treatment response in patients with teriflunomide

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Background and aims: The main goal of this study was to identify the changes in blood immune cells in clinical practice. To predict the treatment response in multiple sclerosis patients treated with teriflunomide.
Methods: RRMS patients who initiated teriflunomide treatment were included in the study. We studied peripheral blood cells obtained before and six months after treatment initiation. Wilcoxon matched pair tests were used to assess differences between basal and one year after treatment results. Correlations were assessed by Kendall's tau-b test.
Results: A total of 86RRMS patients were included. After a year on teriflunomidea treatment, 63 patients showed NEDA and 23ODA. Lymphocytes levels decreased with a mean of 0,553 10^3/uL lymphocytes in 65.1% of the patients at month6. This decrement occurs in 69.6%for ODA(p = 0.004) and 63.5% for NEDA(p=0.000). 69.8%of the patients showed a decrease for leukocytes(mean1,371 10^3/uL) at month six. This decrement occurs in 69.6%for ODA(p=0.080) and 69.8%for NEDA(p=0.001). Monocytes leves increased in 33.7% (mean 0.162 10^3/uL). We observed an increase of monocytes in NEDA patiens 31.7% (p=0.789) and increase of monocytes in ODA patients 39.1% (p=0.170). We did not find a statistically significant correlation between lymphocytes decrement and NEDA (r=0.037,p=0.724), between leukocytes decrement and NEDA (r=0.002,p=0.985) and between monocytes increased and NEDA (r=-0.002,p=0.988).
Conclusion: We observe that teriflunomide induces changes in immune cells in peripheral blood. It was shown a decrease in leukocytes and lymphocytes in both groups and a lower increase in monocytes. We did not find a statistically significant correlation between analytical values and response to treatment.
Disclosure: Nothing to disclose.

EPO-752

The role of magnetic resonance imaging of central nervous system in the diagnosis of primary Sjögren' syndrome

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Background and aims: Neurologic manifestations in primary Sjögren syndrome (SS) described in 15% of patients. Central nervous system (CNS) involvements comparatively to peripheral neurological signs are rarely reported and can precede the sicca syndrome.
Methods: Reviewing retrospectively brain and spine MRI of 21 cases of SS revealed by neurological involvements. Cases were collected from Neurology Department of Military Hospital of Tunis between 2013 and 2020.
Results: Neurological involvement preceded sicca syndrome in seven of 21 cases. Brain MRI was abnormal in 16 patients. Half of lesions were asymptomatic. Spinal MRI was normal in 13 cases despite three cases of clinical medullary syndrome. Gadolinium enhancement was found in 19% of cases. six cases of Brain lesions were punctiform while half of them were nodular. Sub-cortical, peri-ventricular and juxta-cortical were found in eight cases. Spinal cord lesions were nodular in four cases and extensive over more than three vertebras in two cases. Lesions were unique in seven cases Multiple sclerosis-like lesions have been found in eight cases. A radio-clinical correlation was consequently found in 11 cases.
Conclusion: The SS should be considered one of the most frequent syndrome causing inflammatory MRI lesions even in the absence of sicca syndrome.
Disclosure: Central neurological manifestations – Sjögren syndrome –MRI.

EPO-753

Neuro-Behçet disease mimicking brain tumor

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Background and aims: Behçet's disease (BD) is an inflammatory multisystem disease with unknown etiology. In some cases, the disease affects the central nervous system, called Neuro-Behçet Disease (NBD). Few cases of NBD simulating a brain tumor have been previously reported.
Methods: A retrospective study including 35 patients diagnosed with NBD from a population of 150 patients followed for BD was conducted in the department of neurology and internal medicine of the Military Hospital of Tunis from 2000 to 2020. Brain and spinal MRI was performed in all patients with NBD.
Results: We reported three patients with NBD mimicking a brain tumor. The middle age was 41 years old. Mucocutaneous manifestations has been reported in all patients. MRI showed T2hyperintense lesion, larger than two centimeters extending from the medulla to midbrain. Peri-lesional edema with mass effect on surrounding structures was noted in two patients. Brain biopsy rectified the diagnosis in two cases in which neurological involvement was inaugural. The follow-up MRI of these patients showed regression of radiological lesions with steroid treatment.
Conclusion: NBD should be considered as differential diagnosis of brain tumor even when other cardinal manifestations of BD are absent. Mucocutaneous manifestations, eye and joint involvement may be seen less often in these patients.
Disclosure: Neuro-Behçet Disease - brain tumor - MRI

EPO-754

Balancing benefits and risks in treating aggressive MS within COVID-19 pandemic: a single-center experience

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Background and aims: Severe acute respiratory syndrome due to Coronavirus 2 (SARS-CoV-2) pandemic forced deferrals on most of autologous hematopoietic stem-cell transplantation (aHSCT), specifically for autoimmune diseases, in line with European Society for Blood and Marrow transplantation/Autoimmune Disease Working Party indications. Though concerns on the possible repercussions of the infection in transplanted autoimmune patients required higher monitoring, the impending activity that characterizes some forms of Multiple Sclerosis (MS) demanded a special evaluation on the benefit-risk balance. We aim to describe our experience in treating MS-patients with aHSCT along SARS-CoV-2-pandemic.
Methods: Patients candidated to aHSCT were collegially discussed with our haematological and infectious-diseases expertise. two consecutive SARS-CoV-2 negative swabs, a two-weeks-long home-isolation and a five-days intra-department observation were required for treatment start. Patients recently transplanted were all asked to keep safe behaviour and periodically monitored for possible Coronavirus Disease 2019 (COVID-19) symptoms; in particular, those treated in the previous 12-month were asked to maintain a strict home-isolation.
Results: None of the three patients transplanted during pandemic (July, November and December 2020) developed COVID-19. Of the six transplanted in 2019 and that reached one-year from procedure within the outbreak, One developed pauci-symptomatic COVID-19 at the 13th month, confirmed by SARS-CoV-2 swab; white-blood-cells, lymphocyte (totals, CD4+, CD8+ and CD19+) and gamma-globulins levels were normal. two of the remaining 17 patients transplanted from 2015 developed slight COVID-19 symptoms at 30th and 57th month respectively.
Conclusion: Three patients with highly-active MS were treated with aHSCT during pandemic without complications; three minor cases of COVID-19 were recorded in our cohort.
Disclosure: Dr Sbragia E, Dr Boffa G, Raiola AM, Varaldo R, Gualandi F, Angelucci E, Mancardi GL and Inglese M report no disclosures.

EPO-755

Effectiveness, safety and quality of life of adolescent with multiple sclerosis patients treated with fingolimod

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Background and aims: Multiple sclerosis during childhood occurs in 3–10%. Fingolimod (FTY) is a disease-modifying drug recently approved in Italy for treatment of pediatric-MS (Ped-MS) over age 10. We present efficacy/safety profile of FTY in our Ped-MS cohort.

Methods: Demographic, clinical and neuroradiological data were collected from clinical records at San Raffaele Hospital.

Results: Table1 shows demographic, clinical and neuroradiological baseline characteristics of our cohort (8 patients). 50.0% showed clinical and/or neuroradiological activity during follow-up: at month 12, 28.6% presented neuroradiological activity and none had relapses. At month 24, all patients were free from both clinical and neuroradiological activity. Mean Annualized Relapse Rate (ARR) at months 12 and 24 were 0.68 and 0.35 and median Expanded Disability Status Scale (EDSS) was 1.0 at both time points. No patients presented EDSS progression during follow-up. two patients switched to natalizumab for persistent MRI-activity at months seven and eight: both were highly-active at onset and showed the highest baseline ARR scores. Patients' quality of life (QoL) at month 12 was measured by administering Pediatric Quality of Life (PedsQL) Inventory, Italian-version-4.0. Mean+standard deviation Total, Physical-Health and Psychosocial-Health scores were 77.9+5.9, 81.7+11.0 and 75.7+6.2, respectively. None of the patients reported side effects. Mean+standard deviation absolute lymphocyte counts at months 12 and 24 were 562 and 557.5 cell/mm^3.

N=8	F= 6; 75%
Age at MS onset (y), mean ± SD (min-max)	14,5 ± 2,3 (11,4-17,2)
Functional System involved at onset, N (%)	- **S=** 1 (12,5%) - **B=** 4 (50%) - **P=** 2 (25%) - **V=** 1 (12,5%)
Time from onset to FTY start (m), mean + SD (min-max)	13,0 + 11,7 (4,3-36,6)
EDSS, median (min-max)	1,5 (1,0-2,0)
ARR (mean) ± SD, at baseline	3,0 ± 1,3
Treatment characteristics	**Naive**= 5 (62,5%) **Switch from 1° line DMDs** = 3, (37,5%) - **switch from IFN,** = 2, (66,7%) - **switch from BG12** = 1 (33,3%)
Brain T2-weighted lesion count, mean (min-max)	16,1 (4,0-48,0)
Brain Gadolinium-enhancing lesion count, mean (min-max)	2,8 (0,0-13,0)
Spinal cord T2-weighted lesion count, mean (min-max)	2,3 (0,0-8,0)
Spinal cord Gadolinium-enhancing lesion count, mean (min-max)	0,3 (0,0-1,0)
Follow-up (m), mean ± stand dev (min-max)	22,9 ± 7,3 (8,5-31,6)

Table 1. Demographic, clinical and neuro-radiological characteristics of population at baseline.

Conclusion: Ped-MS subjects overall benefited from FTY, which was also well tolerated. Moreover, our patients referred a good QoL. Our data support FTY use in this special population avoiding highly active patients. Further evidence and longer follow-up are needed to confirm our observations.

Disclosure: CZ has no disclosure. LM received compensation for speaking from Biogen, Merck-Serono, Novartis, Roche, Sanofi. MF received compensation for consulting/speaking from Biogen, Merck-Serono, Novartis, Teva, Roche.

EPO-756

Inflammatory? Neoplasic? Why not both? A Case report of concurrent Glioblastoma and Multiple Sclerosis

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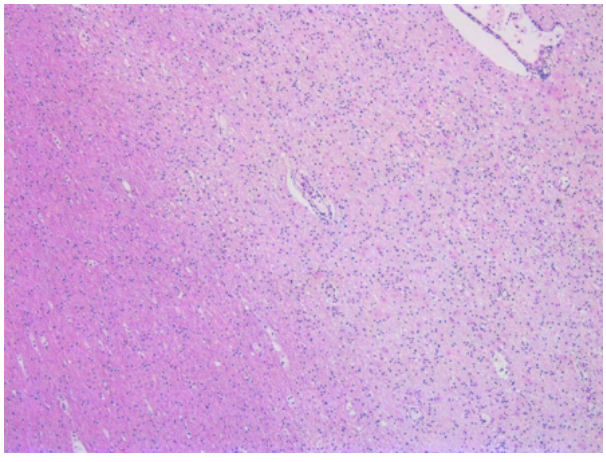
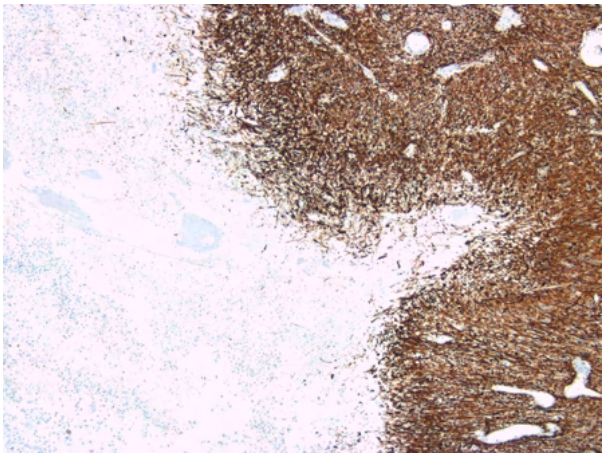
Background and aims: We present a case of undiagnosed multiple sclerosis (MS) presenting with focal seizures and space-occupying lesion.
Methods: Not applicable.
Results: A 39-year-old woman presented with focal seizures on the right hemiface and upper right limb with retained awareness. At the age of 19 she had an episode of right facial palsy with one week duration and, at 29, a 24-hour episode of gait imbalance. The neurological examination disclosed right central facial palsy, dysarthria, transcortical motor afasia and mild right upper limb paresis. Brain MRI showed multiple demyelinating lesions, two with ring gadolinium-enhancement and another corticosubcortical lesion at the left pre-central convexity with solid heterogeneous gadolinium-enhancement. Spine MRI T2 and STIR revealed a non-enhancing T6 centromedular hyperintense lesion. Cerebrospinal fluid revealed nine leucocytes with mononuclear predominance and intra-tecal IgG synthesis with oligoclonal IgG bands. Serum tests were negative. Treatment with triple antiseizure therapy, methylprednisolone and immunoglobulin was needed to achieve seizures control. At reevaluation, there was clinical and imagiological worsening which prompted treatment with plasma exchange. Unfortunately, due to a possible procedure-related complication, the patient died. Histologic sections from the brain autopsy revealed glioblastoma and MS.



Demyelinated area with macrophagic cells



Glial cell proliferation with necrous areas – highly suggestive of glioblastoma

Conclusion: This case emphasizes the importance of excluding other diagnosis in patients with MS especially if there are long relapses and refractory to immunomodulatory treatment, steady clinical deterioration or uncommon features of MS, like seizures. Efforts should be provided in order to exclude concurrent pathologies and also to better differentiate from rarer forms of MS, such as the pseudotumoral type, even if there is need to brain biopsy.
Disclosure: Nothing to disclose. .

EPO-757

Dysphagia and quality of life in multiple sclerosis patients

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Background and aims: Dysphagia is a common disabling symptom which can lead to serious complications and can affect the quality of life of the patient. Regular screening and diagnosis of dysphagia in patients with multiple sclerosis are important and crucial.
Methods: The paper aims to analyze the presence of the dysphagia and to identify the relationship between it and quality of life on patients with multiple sclerosis (MS). 41 patients diagnosed with MS have been clinically evaluated using Expanded Disability Status Scale (EDSS). We applied specific dysphagia tools: Dysphagia in Multiple Sclerosis Questionnaire (DYMUS) and Eating Assesment Tool (EAT). Quality of life was measured by the self-reporting scale: EuroQol five-Dimension, with EQ-5D-index and EQ-Visual Analogue Scale (EQ-VAS).
Statistical correlations were performed.
Results: 26 patients were females (63,4%) and 15 patients were males (36,6 %). Almost 40% of patients reported dysphagia according to all applied dysphagia scales. The dysphagia tools (DYSMUS and EAT) correlated statistically significant with EDSS ($p < 0{,}001$) and self reported scale EQ-5D correlated statistically significant with all applied dysphagia scales ($pD = 0{,}0005 < 0{,}001$ and $pE = 0{,}00008 < 0{,}001$).
Conclusion: DYMUS and EAT demonstrated to be easy and consistent tools to detect dysphagia on patients with multiple sclerosis. The quality of life on patients with multiple sclerosis depends on swallowing disorder. Those patients with dysphagia have higher physical disabilities.
Disclosure: Nothing to disclose.

EPO-758

Clinical and radiological phenotype of Multiple Sclerosis associated to Coeliac Disease: a monocentric experience

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Background and aims: Multiple Sclerosis (MS) may co-occur in subjects with coeliac diseases (CD). However, it is not clear if it shows distinctive clinical features compared to MS occurring in non-CD subjects and if it should be considered as part of extraintestinal CD spectrum.
Methods: We retrospectively analyzed clinical, radiological and genetic variables in 18 MS+CD patients positive for serological, histological and genetic CD markers and 17 MS patients with risk factors for CD (CRF) such as being CD first-degree relatives or complaining CD symptoms, compared to 18 MS patients and eight Neuromyelitis optica spectrum disorder (NMOsd) patients.
Results: Optic neuritis (ON) and myelitis were the most common presentations at disease onset among MS+CD (38,89% and 50%) MS+CRF (24% and 41%) and NMOsd patients (50% and 50%), compared to MS (11% and 28%). Using Kruskal-Wallis test and Bonferroni correction, similar pattern was observed along disease course for MS+CD compared to MS (84% vs 50%, $p<0.011$ for myelitis, 50% vs 22%, $p=0.227$ for ON). The predictive numbers of spinal cord lesions at MRI onset was higher in MS+CD ($p<0.01$) and NMOsd compared to MS patients. Using a Poisson distribution and considering the whole population, high risk HLA DQ2/DQ8 genotypes were significantly associated with myelitis ($p<0.002$).
Conclusion: ON and myelitis characterize the clinical phenotype of MS+CD and MS+CRF patients. Screening for CD should be included in differential diagnosis work-up in case of newly diagnosed MS patients predominantly showing these clinical features. Further studies will clarify if MS associated with CD should be considered a new disease entity.
Disclosure: Authors have nothing to disclose.

EPO-759

Multiple Sclerosis in Pregnancy: A single centre multidisciplinary experience

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Background and aims: Multiple sclerosis (MS) may stabilise or improve during pregnancy, but relapse risk increases postnatally. Given the complexity of current disease-modifying drugs (DMDs) used in MS alongside complex maternal care, we analysed MS relapses (MSR) in patients seen by our neuro-obstetric multi-disciplinary team.
Methods: Retrospective study at Queen Charlotte's and Chelsea Hospital, UK, 2012–2020, of pregnancy encounters (PEs) where MSR occurred during pregnancy or up to one-year postnatal (PN). 40 patients identified with MS with varying severity. Data collected for: socio-demographics; parity; maternal and neonatal outcome; expanded disability status scale score (EDSS); MSR; DMDs; pre-pregnancy counselling (PPC).
Results: In 51 MS PEs, 10% were referred for PPC. 44 live births; mean birth gestation 38 weeks. 25% C-section rate in MS compared to 27.9% overall. Average EDSS 1.6 pre-pregnancy and 1.8 PN. EDSS increased in 27% of PEs either during pregnancy/PN. At least one radiological or clinical MSR was documented in 46% of PEs. Total 31 PEs DMDs used pre-pregnancy: 24 paused DMDs; seven continued DMDs (natalizumab/ glatiramer) during pregnancy. Where DMDs continued in pregnancy, 43% had at least one MSR compared to 48% in those who discontinued medication. No correlation between MSR and EDSS statistics.
Conclusion: MS patients EDSS score deteriorates PN. Those with moderate to severe disease should be referred for PPC for advice regarding optimising DMD use pre-pregnancy and continuation in pregnancy to limit relapses. Women with MS have similar pregnancy outcomes to those without. Multidisciplinary neuro-obstetric clinics are ideal for PPC and managing pregnant MS women in pregnancy.
Disclosure: No disclosures.

EPO-760

COVID-19 infection and vaccination in patients with multiple sclerosis during COVID pandemic

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Background and aims: Patients with multiple sclerosis are treated with immunomodulatory and immunsuppresive treatments. Due to the outbreak of the pandemic, the management and treatment of our patients was a challenge, Objective : to study MS patients with Covid-19 and the first vaccinated patients.
Methods: Prospective study. We analyzed the demographic characteristics, symptoms and treatment of Covid-19 infection and MS treatment.
Results: 35 MS patients were infected with Covid-19 during the first wave . Average age was 40 years old with a disease duration of 10 years and an average EDSS of 2.5. 28 have a RRMS, three SPMS, two PPMS. 18 were confirmed by PCR ir serology and four by radiologic criteria. Only five patients were hospitalized and one of them died (EMSP, EDSS :8). 30 patients have a mild or very mild infection course. 31 patients were under MS treatment (48% highly active treatment). Three treatments were delayed 10 days and five treatments four weeks. The most frequent symptoms were fever, cough, dyspnea, fatigue. The infection duration were between one and seven weeks. 12 MS patients treated with DMTs received the first shot of mRNA vaccination without severe adverse events.
Conclusion: MS patients have a similar evolution of Covid19 infection as healthy subjects. No MS treatment was related with worse outcome. Most of patients had continued the DMTs. It seems that the vaccination is safe for MS patients.
Disclosure: Speaking and/or consultancy fees (Bayer, Biogen, Merck Serono, Novartis, Roche, Sanofi, and Teva).

EPO-761

Russian e-Registry of patients with multiple sclerosis: highlights of a three-year study

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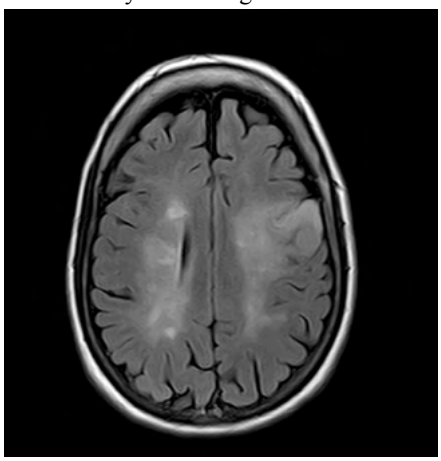
Background and aims: The prevalence of multiple sclerosis in the Russian Federation varies from 10 to 80 people per 100,000 depending on the geographic area. Conduction of large-scale epidemiology studies is a promising approach in establishing risk factors that lead to a more severe disease course, as well as defining treatment needs in various country regions. In 2017, an electronic registry of adult patients with multiple sclerosis (MS) that live in Russian Federation was initiated. We present results of a three-year experience of maintaining a Russian e-Registry of patients with MS.
Methods: The Russian MS e-Registry is a prospective multicenter non-interventional study with a retrospective analysis of available medical records at the time of the patient's enrollment. A special individual registration form was created in order to collect both clinical, instrumental and epidemiological data.
Results: Between December 2017 and December 2020, data on 3,028 patients with MS were collected. The following information was obtained: basic demographic statistics, extensive clinical data such as disease course and duration, diagnosis at the moment of symptom onset and time of confirmed diagnosis, number and nature of disease exacerbations, EDSS, use of disease-modifying therapies (DMTs) and switching between different DMTs; results of multiple laboratory findings, including oligoclonal bands in cerebrospinal fluid, and MRI data throughout the disease course.
Conclusion: Our findings suggest that several major issues, such as delayed MS diagnosis and late initiation of DMT, as



well as incorrect switching between different DMTs can contribute to earlier transition of
relapsing-remitting MS to a secondary progressive course.
Disclosure: The authors have no conflicts of interest to declare.

EPO-762

Assessment of balance impairment in multiple sclerosis with NIH Toolbox Standing Balance Test

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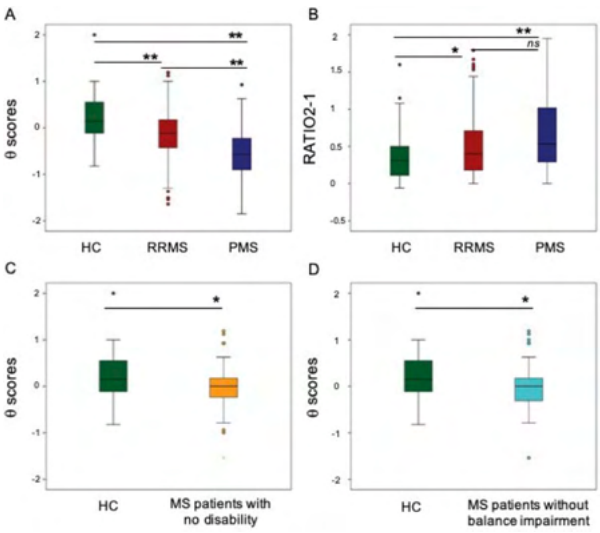
Background and aims: To test the hypothesis that NIH Toolbox Standing Balance Test (SBT) is able to detect mild balance impairment in patients with multiple sclerosis (MS) and is more sensitive than clinical evaluation according to the Expanded-Disability-Status-Scale (EDSS).
Methods: 186 patients with MS (83% relapsing-remitting MS) and 70 healthy controls (HC) were prospectively enrolled and underwent Expanded-Disability-Status-Scale (EDSS) evaluation and NIH Toolbox SBT. Differences in balance metrics, including theta score (a global metric of balance performance, in which higher values reflects better performance), were assessed. Balance metrics were corrected for age, sex, height and weight.
Results: MS patients had significantly worse balance performance compared with HC, with patients with progressive MS having the lowest scores. MS patients with EDSS≤1.5 and patients without any evidence of balance impairment (score of 0 in the brainstem, cerebellar and sensory EDSS-functional systems) had still worse balance scores than HC. The pyramidal, brainstem and cerebellar domains were selected as the most sensitive to theta metric variance. A cut-off theta value of 0 had a 73% sensitivity and a 61% specificity in correctly classifying MS patients from HC.



Figure

Conclusion: NIH Toolbox SBT is able to detect, on routine examination, quantitative balance alterations in MS patients with a low burden of disability and it is more sensitive than EDSS balance-related functional domains. **Disclosure:** M.Inglese received grants NIH, NMSS, FISM; received fees for consultation from Roche, Genzyme, Merck, Biogen and Novartis.

EPO-763

Hemianopic defects as a manifestation of multiple sclerosis relapse

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Background and aims: While visual impairment in multiple sclerosis (MS) is frequently caused by optic neuritis, up to 10% of patients evidence asymptomatic retrochiasmal visual field defects (RVFD). Symptomatic RVFD on the other hand are believed to be rare. We describe a series of four MS patients whose relapse consisted of a symptomatic RVFD.
Methods: Analysis of patients records and investigation results.
Results: Case 1: A 24-year-old female presented with one-month bilateral visual loss. Perimetry revealed an incongruous right homonymous hemianopia. MRI revealed demyelinating gadolinium-enhancing (Gd+) lesions, including one in the left optic tract, leading to MS diagnosis. Case 2: A 37-year-old female, with a nine-year diagnosis of MS, presented with three-day blurred vision bilaterally. Perimetry revealed a congruous incomplete left superior homonymous quadrantanopia. MRI revealed demyelinating lesions including one Gd- lesion involving the right temporal optic radiation. Case 3: A 34-year-old female, with a six-year diagnosis of MS, presented with asymmetric blurred vision. Perimetry revealed a left superior homonymous pericentral quadrantanopia. MRI revealed a Gd+ right posterior temporal lesion. Case 4: A healthy 42-year-old female reported three-month blurred vision bilaterally. Perimetry was normal but optical coherence tomography revealed decreased ganglion cell thickness with a left hemianopic pattern. MRI revealed an old left optic tract demyelinating lesion. Before perimetry, none of these patients had a RVFD suspicion, nor was RVFD detected at the bedside.
Conclusion: Despite rare, RVFD should be considered in all MS patients with visual complaints. Perimetric and OCT assessment is critical for a timely diagnosis.
Disclosure: Nothing to disclose.

EPO-764

Ocrelizumab – time to expand borders?

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Background and aims: Ocrelizumab's trial ORATORIO for Primary Progressive Multiple Sclerosis (PPMS) included a selected subgroup of young participants. We aimed to evaluate this treatment's results in a real-life setting, where patients often do not meet ORATORIO's inclusion criteria.
Methods: Retrospective cohort study including all PPMS patients with at least two Ocrelizumab cycles followed until December 2020 at two centers. two groups were defined: a control – aged 18–55 years, baseline EDSS 3–6.5, symptom duration <15 years for a baseline EDSS>5 or <10 years if baseline EDSS<5 – and an expanded group – if any of the criteria was not met. Groups were compared through chi-squared and t-student tests. Efficacy and safety outcomes were analyzed with a chi-squared test; additionally, time to EDSS progression was assessed using a Cox regression with a log-rank test.
Results: We included 51 patients, 39.2% women, median age at first infusion 51 (28–72) years, symptom duration eight (1–24) years. Median follow-up time was 19 (6–31) months. The majority (n=35, 68.6%) belonged to the expanded group, with significantly older patients (p=0.037) and longer disease duration (p<0.001). No difference was observed in EDSS progression (31.2% control, 34.2% expanded, p=0.831) nor in time until EDSS progression (HR 0.931, CI 95% 0.324–2.683, p=0.896) between groups. Secondary outcomes (Timed-25-Foot-Walk, 9-Hole-Peg Test, MRI activity) were similar (0.09<p<0.932), just as incidence of any adverse event (31.3% control, 22.9% expanded, p=0.523).
Conclusion: We found no significant difference in efficacy and safety outcomes between groups. Findings suggest a benefit of extending the indication of Ocrelizumab beyond the trial's inclusion criteria.
Disclosure: Nothing to disclose.

EPO-765

Comparative study between Neuromyelitis Optica seropositive patients and seronegative patients : a Tunisian study

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Background and aims: Neuromyelitis optica (NMO) is an inflammatory disorder characterized by recurrent optic neuritis (ON) and transverse myelitis(TM). The anti-aquaporin-4 (AQP4) antibody, has been claimed to play a pathogenic role in NMO and can be used to achieve an early diagnosis. However, some patients remain seronegative despite a definite diagnosis of NMO.
Methods: We collected in the national institute of Tunisia 42 patients with NMO. We described and compared epidemiological clinical, radiological features and outcome of NMO(+) et NMO(-).
Results: In our study 26 patients were NMO(+) and 16 patients were NMO(-). Seronegative patients exhibit a low female/male ratio (1,6) compared to seropositive (12). The mean age of onset was 38.25 years for seronegative and 36.19. Simultaneous ON and TM at onset is marquely higher in NMO(-) group (33.3% vs 4.3%, p=0.017). Initial EDSS tend to be similar in both groups (2.5 à 3). Almost all patients presented relapses with higher rate for seronegative patients (two/year vs one/year). Radiologic study revealed more frequent supratentoriel lesions for NMO(-) than NMO(+)(60% vs 40%). Relapses were treated with intravenous corticoid for all patients. Plasmapheresis and intravenous Immunoglobulin were prescribed in both group. Recovery was noted in two third of patients in both groups. Most of patients were treated with oral corticoid and immunosuppression treatment. The mean EDDS at the last follow was three for NMO- and four for NMO+.
Conclusion: The results of our study match the data of literature with low female/male ratio, age at onset often higher in NMO(-), more frequent simultaneous ON and TM at onset and more frequent supratentorial lesions in MRI for seronegative group. There was no significant differences in treatment response or the clinical course between both group.
Disclosure: Nothing to disclose.

Neurology and arts, History of neurology, Education in neurology

EPO-766

Brainpainneuro and the role of Instagram in science communication: Experience Report

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Background and aims: Neurosurgery is a medical specialty that aims to treat pathologies that affect the central and peripheral nervous system. The creation on July 2, 2020 of Instagram entitled @brainpain_neuro made it possible for academics to get in touch with the area, classes on neurosurgical themes and scientific immersion. The purpose of this work is to report the experience with the @brainpain_neuro profile created on Instagram.
Methods: It is an experience report, which members show themselves immersed in the scientific environment, through the organization of classes on the most relevant topics in neurosurgery, in addition to a vast scientific production.
Results: Since its creation, @brainpain_neuro has published 33 Instagram posts in the areas of Neurology and Neurosurgery, such as Deep Brain Stimulation, chronic pain, neuroimaging, stroke and hydrocephalus. Held five online classes on neurology topics, with the target audience composed of members and medical students. In scientific production, five oral presentations in English and Portuguese, in scientific congresses, two congress posters, one e-book and one article were made, within the most varied topics of neurosurgery and neurology.
Conclusion: The creation of an Instagram profile focused on a specialty enables a new and easy immersion of academics with that interest, allowing to create new opportunities that expand beyond the university center in which the individual is installed. Thus, it is important that we can expand the use of Instagram and take advantage of the possibilities that social networks bring to teaching and creating opportunities within the academic area.
Disclosure: The authors have no conflicts of interest to declare.

EPO-767

Virtual education in the time of COVID-19 pandemic

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Background and aims: Due to COVID-19, neurological congresses were cancelled or shifted to the virtual environment. The virtual environment may require expensive technical solutions, or we may use video communication software. Our study aimed to evaluate the satisfaction of doctors with participation in virtual education.
Methods: 200 doctors participated at regional vascular neurology congress, broadcasted via Zoom. Congress lasted eight hours. After the congress, participants filled out an online evaluation.
Results: 146 participants (73%) replied to our survey. 79% were specialist, 12% residents and 9% retired physicians; 33% of all participants were neurologists. 32% listened to all lectures, and 54% listened to more than half. 66% intend to watch at least some of the talks stored in the online database. On the scale from one (not satisfied) to 10 (very satisfied), 76% gave eight or more for the interaction with the speakers and other participants, 88% for obtaining new information, 97% for the topics presented at the congress, and 90% for overall all evaluation of the congress. Most participants would like to have a hybrid meeting in the future (43%), 22% prefer a virtual meeting, while only 35% wish to attend in person.
Conclusion: Our results demonstrate that we can successfully organize smaller meetings using simple conference software. The congress program may be more important for the participants, than the place of venue. In the future, we may expect more hybrid meetings.
Disclosure: Nothing to disclose.

EPO-768

DMD Care UK: implementation of the latest standards of care across the UK

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Background and aims: In 2018 a significant update to the Duchenne muscular dystrophy (DMD) standards of care (SoC) was published in the Lancet Neurology. The updated SoC are ambitious and significantly advance on those from 2010. This presents challenges at a national level where the health care systems need to increase or change provision. To address this, Duchenne UK, North Star and Newcastle University have worked together to launch the DMD Care UK project (www.dmdcareuk.org).
Methods: In order to reach national consensus and address inequalities, expert working groups (WGs) mirror the SoC areas and will: · Establish how SoC is currently delivered at centres in the UK · Consult with expert centres across North Star and patient groups to reach consensus on UK-specific recommendations. · Formulate a prioritised short, medium and long-term plan to implement these · Work with the patient community to generate 'patient-friendly' information · Collaborate with adult North Star recommendations · Identify needs for additional evidence to support decision making and propose/address research questions The next phases will focus on implementation.
Results: WGs have been established in several areas and are active. The Bone and Endocrine WG has reached consensus on recommendations, achieved professional body endorsement, produced patient information booklets, conducted webinars and worked on the distribution of steroid alert wristbands. Other WGs are following a similar model.
Conclusion: This project represents a collaboration and willingness to work together across different stakeholders, all with the same aim – to improve the standard of care and therefore the lives of people living with DMD in the UK and their families.
Disclosure: My salary is funded by Duchenne UK who are partners in this project.

EPO-769

Connecting women in neurosciences (CWIN) – a peer-lead networking project among young, female, clinical neuroscientists

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Background and aims: Simultaneously acquiring broad clinical knowledge and scientific expertise is a major challenge for young clinical scientists. Additionally, female researchers may face hurdles e.g. due to unconscious bias. We aimed to address professional and gender-related challenges in a protected environment among junior female clinical neuroscientists.
Methods: We implemented a peer-lead networking group to increase clinical and scientific knowledge, improve soft skills and encourage exchange between fellow female residents. During monthly meetings, two participants hold short presentations on a clinical topic or scientific method, followed by a discussion and feedback to the presenter. Afterwards, participants networked and discussed different challenges. The Covid-19 pandemic required holding some of the meetings virtually.
Results: Nine female neurology residents at a Swiss University Hospital with three years of clinical training participated in the "Connecting Women in Neurosciences" (CWIN) project, which started in August 2020. Participants felt empowered by these meetings and profited from their new network in their clinical and research activities. During the meetings, we identified several challenges, some of which participants perceived to be gender-related (e.g. assertiveness).
Conclusion: Peer-to-peer networking is an easy and low-budget intervention to encourage female residents to engage in research activities, profit from each other's expertise and promote interdisciplinary teamwork. A project like CWIN provides a protected environment to discuss and overcome challenges related to personal and social expectations, some of which are gender-related. We encourage young colleagues to engage in structured networking activities with their local peers.
Disclosure: This project was supported by a grant by the University of Bern («Nachwuchsförderungs-Projektpool») in June 2020.

EPO-770

Health Information Technology Competencies in the European Neurology Residency Curricula

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Background and aims: Neurology has already integrated many new technologies in its daily practice. The growing adoption of digital health technology should be complemented with better education in Health Information Technology (HIT) competencies in neurologists. Here, we aim to compare the current learning objectives of the European neurology residency curricula with the HITComp framework of the EU-US eHealth Work Project.
Methods: The European Training Requirements for Neurology (ETRN) published by the UEMS were reviewed as the primary source about the required and preferred content of residency curricula in Europe. Additional information was gathered through a review of the available literature. The specified competencies were then compared against the proposed competencies for Physicians in HITCOMP in order to notice overlaps and potential deficiencies.
Results: HITCOMP specifies 64 competencies essential for Physicians. Eight of these are institution- or country-specific. Of the 56 remaining, two were found to be directly obtainable from the specific learning objectives in the ETRN. Eight are directly connected to ETRN objectives, but are not explicitly mentioned. 13 are considered to be only alluded to. All in all, while the ETRN calls for the provision of digital skills, no specific objectives are set.
Conclusion: There is a large drive for innovation in Neurology, especially with the emergence of personalised treatments, patient apps and more. The need for more structured approaches to education in HIT competencies is evident and appears to be widely understood, even if not directly implemented right now. This should be changed so that the field can continue to integrate innovations efficiently.
Disclosure: No disclosure necessary.

EPO-771

Engaging the Alzheimer's disease (AD) CareRing caregiver community in designing the Phase IB/IIA Brainshuttle AD trial

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Background and aims: Clinical trial participation often involves more than patients, especially for neurological conditions such as AD, where it can also heavily impact the caregivers and families providing support before, during and after study visits. To enable the design of trials that are less burdensome for participants and caregivers, the CareRing initiative explored: participant/caregiver motivations and expectations for early-phase clinical trials not designed to demonstrate treatment benefits; the role caregivers may play if a loved one participated in such a trial; and collaborative approaches to developing trial protocols and co-creation of materials that allow the target population to participate with minimal impact on daily life.
Methods: Roche employees from different geographical regions, with varying backgrounds and roles, who are caregivers for someone with AD, participated in two 60-minute telephone calls. The calls introduced the draft protocol for the Phase IB/IIA Brainshuttle AD trial evaluating brain-shuttle gantenerumab in prodromal or mild-to-moderate AD (NCT04639050), and allowed caregivers to provide input on the protocol and holistic support that could alleviate the burden of participation for participants and caregivers.
Results: Guidance on trial design and holistic support for caregivers and families will be developed based on the caregivers' recommendations.
Conclusion: The CareRing initiative allows us to collaborate with caregivers to design early-phase clinical trials that meet participant and caregiver needs, while also answering scientific questions. Early engagement with the broader patient community will help ensure trial designs enable the target population to participate should they wish. Established internal networks can support this type of initiative.
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EPO-772

Monosynaptic Reflexes MSR, the first parameter for psychophysiological activation - History, methods, results

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Background and aims: Little is known of MSR studies of activation, the first activation parameters (since 1887).
Methods: An overview on the history of methods in psychophysiological reflex studies is given from literature (1887 to 1985).
Results: Lombard (1887, AmJPsychol, vol. one) used a hammer with defined drop height and registration of "knee jerks" in single proband studies (e. g. under fatigue, exciting vs. relaxing pieces of music). Bowditch & Warren (1890) elicited reflexes and preceding stimuli by a complicated apparatus, and showed phasic activation after different stimuli (auditory, visual, touch) in the time up to 2,000ms (as known from other activation parameters). Paillard (1955) registered simultaneously T-reflexes, elicited by an electromagnetic hammer, and electrically evoked H-reflexes of triceps surae muscles. Reflex amplitudes were read from the oscilloscope. T-reflexes generally were more reactive than H-reflexes. But one proband was able to reduce T- and H-reflexes in kind of biofeedback, when watching the oscilloscope. Following researchers (Bathien and his group 1969, 1971; Brunia 1970, 1971) showed elevation of T-reflexes under activation, H-reflexes being not or less reactive. Sczesni & Kröner (1985) used T-reflexes and galvanic skin responses (GSR) under activation by a task, compared to naive or autogenic relaxation.
Conclusion: For about a 100 years reflex (MSR) studies were used in testing psychophysiological activation. Tonic as well as phasic activation had been studied. T-reflexes proved to be more sensitive than H-reflexes. They were the first parameters used in this field. Presumably the vast technical equipment had limited its further use..
Disclosure: No conflicts, nothing to declare.

EPO-773

The dendroarchitectonics of E. Ramón-Moliner

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Background and aims: Neurons can be characterized by their degree of morphological configuration patterns/ specialization.
Methods: Review of the dendroarchitectonics of E. Ramón-Moliner in the vertebrate nervous system (1962, 1967, 1968, 1975, with W. J. H. Nauta 1966), comparison with S. Ramón y Cajal's work (1904; 2002: translated by P. and T. Pasik).
Results: 1. three principal neuronal types: isodendritic (undifferentiated), allo- and idiodendritic neurons (intermediate and high specialization, resp.). "Isodendritic core": overlapping areas (brainstem and adjacent areas, about the "reticular formation"). "Leptodendritic core" within the isodendritic core: most primitive cells (periventricular or subependymal regions). Allo-/ idiodendritic neurons appear very early in embryonary life (long ahead invaded by afferent fibers). 2. two main types of neurons in a projected primordial brain: lophodendritic cells (apical dendrite and subpial tufts); leptodendritic (slender) neurons. 3. three stage-scheme of the reconstructed/projected phylogenetic history: primordial stage I, periventricular leptodendritic cells and subpial lophodendritics intermingled, also isodendritic motor neurons; stage II, progressive separation of periventricular and subpial layers, segregation of neurons with the specialized dendritic pattern; stage III, final dendroarchitectonic pageantry with two main trends: telencephalic trend (according to Ramón y Cajal), responsible for the distribution neurons with subpial dendritic tufts (cortical pyramidal cells); rhombencephalic trend, a transition from leptodendritic/isodendritic to idiodendritic neurons, preservation of primordial/ pluripotential core.
Conclusion: Ramón-Moliner reconstructed the projected phylogenetic history that led to dendroarchitectonic families employing a three-stage scheme. Embryonically, increasingly specialized, allo-/idiodentric neurons appear long before particular functional attributes can be implicated. Therefore, he rejected ontogeny as a recapitulation of phylogeny in contrast to Ramón y Cajal's parallelism of the two.
Disclosure: Nothing to disclose.

EPO-774

Frontotemporal dementia, art, and biography: course of a life

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Background and aims: I report the biography and natural history of an elderly emergent artist who developed frontotemporal dementia (FTD).
Methods: Biographical and disease history taking, clinical examination, neuropsychological testing, and neuroimaging were employed.
Results: Although this female patient always enjoyed painting, she did so very little in her younger adulthood. Shortly after the age of 56, when her last child moved out of the house, she started to paint intensively ("for her father") and attended art classes. She was concerned with her father, who had returned as a broken man from World War II captivity and was hitting her mother when drunken. At the age of 75, personality changes, and at 78, memory defaicits became apparent. Painting stopped at 79. During her painting period, three-dimensionality and detail became reduced, while contrast and colour spectrum increased. Aged 81, she was diagnosed with the behavioural variant FTD. She showed perseveration/circumstantial speech, and incoherence of thoughts, disinhibition, and emotional lability. Neuropsychological testing revealed reduced semantic word fluency, verbal new memory formation, and retrieval and recognition of spoken content. There were also executive dysfunction and deficits in visuo-constructive skills and the retrieval of non-verbal content. A computed tomography scan showed bilateral (left>right) frontotemporal atrophy.
Conclusion: Biographical and neurobiological factors may contribute to emergent artistic creativity in FTD and related symptoms, be it as an expression of the inner life or an attempt of compensation in the face of evolving disease. Therefore, understanding a patient's potential is crucial for art therapy tailored to individual needs.
Disclosure: Nothing to disclose.

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