

ePoster Session

Saturday, 24 June 2017

Ageing and dementia 1

EP1001

ASL MRI in early diagnosis of Alzheimer's disease: A biomarker suitable for clinical settings?M.H. Alpsan Gokmen¹, M. Dokdok², Y. Kutukcu¹, K. Karaman², O. Karadeniz²¹Neurology, Anadolu Medical Center, Kocaeli, Turkey,²Radiology, Anadolu Medical Center, Kocaeli, Turkey,

Background and aims: Early diagnosis is very important in Alzheimer's Disease as the pathological process, starts years before cognitive impairment gets attention and the patient seeks medical advice. ASL MRI (Arterial Spin Labeling) is a functional MRI, which is a quick and a relatively cheaper method. Also it is safer as it does not require a radioactive material or a contrast agent injection.

Methods: In our study, we used ASL MRI as an early biomarker in patients with cognitive problems. 85 patients were included and 24 of patients had MCI (minimal cognitive impairment), 23 had Alzheimer's Disease, 31 of the patients were diagnosed as having depression and 7 of the patients had subjective memory impairment (SMI).

Results: Bilateral parietal hypoperfusion pattern were found statistically significantly more in the AD and MCI group than depression and SMI group ($p < 0.001$). Additionally a difference, which was significant, was found between MCI and AD. Hypoperfusion rates were 67% among MCI and 83% in AD group. Hypoperfusion rate of ASL maps in depressive patients who did not show cognitive deficits according to neuropsychiatric evaluation was 13% which was significantly lower than MCI and AD groups and similar to the subjective cognitive deficit group (SMI) who also did not show any cognitive deficit in Neuropsychiatric tests.

Conclusion: This study shows that ASL MRI is quick, cheap and easy to access in a clinic where MRI is available. It is a valuable method in early evaluation of cognitive deficits and differentiation of the pathology which causes forgetfulness.

Disclosure: Nothing to disclose

EP1002

A trend towards associative binding impairment but not delayed recall impairment of explicit memory by healthy aging decliners vs supernormals: Preliminary dataO. Bezdicek¹, M. Cervenkova¹, H. Stepankova¹, B. Schmand², H. Buschke³, T. Nikolai⁴, A. Rulseh⁵¹National Institute of Mental Health, Prague, CzechRepublic, ²Psychology, University of Amsterdam, Amsterdam,Netherlands, ³Albert Einstein College of Medicine, YeshivaUniversity, New York, USA, ⁴Department of Neurology, 2nd

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Background and aims: We endeavored to investigate if we can find predictors of cognitive decline in healthy aging. Specifically, we wanted to examine Benjamin-Naveh's associative-deficit hypothesis (ADH) in episodic memory: a major factor in older adults' poorer episodic memory is their deficiency in creating and retrieving links between the representation of two mental codes.

Methods: Healthy participants were followed with cognitive test measures for four years. Afterward, we aimed to compare supernormals ($N=20$; $(73.9 \pm (SD)7.7$ years)) with decliners ($N=6$; $(75.8 \pm (SD)8.0$ years)) and we wanted to find out if the decliners will show abnormal rates of cognitive decline in episodic memory and brain atrophy. Measures of brain volumes derived from 3 Tesla magnetic resonance imaging scanner (MRI) were acquired, and an automated system (FreeSurfer) was used for further analyses.

Results: Regarding explicit memory measures we found only a trend towards difference based on Mann-Whitney U test between supernormals and decliners in Memory Binding test, an associative binding measure ($p=.072$, one-tailed), other measures, such as Philadelphia Verbal Learning Test or Logical Memory delayed free recall were not significant ($p > .10$). Automated segmentation by FreeSurfer (version 5.3) did not reveal any groupwise volumetric differences between supernormals and decliners.

Conclusion: There is a trend towards significance in associative binding impairment in healthy aging decliners in comparison to supernormals despite non-significant differences in their brain volume. The data are consistent with Benjamin-Nave's ADH. However, these preliminary results need to be taken with caution and replicated on larger samples.

Disclosure: Supported by the grant "Cognitive Predictors of Neurodegeneration from the Czech Science Foundation," under grant number 16-01781S.

EP1003

Cancelled

EP1004

Computerized attention test web based (CVST) as the key to a screening tool for attention and cognition deficits (http://neurocenter.nl/en_GB)

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Background and aims: The perspective of effective treatment of neurodegenerative cognitive disorders implies an early intervention and therefore a reliable, easy screening tool.

Methods: Clinical neurological experience of over 25 years with regards to early detection and evolution of cognitive impairment by computerized screening tools, was extracted out of a private practice database. Determining cut-off scores for pathology. Explanation of mechanisms leading to false positive results.

Results: Matching of this screening exam with the M.M.S.E., the neuropsychological testing, imaging and the liquor analysis (beta amyloid, tau - fosfotau protein) was done for all diagnosed cases. A normal CVST score lies between 8 and 13 seconds. With a score above 20 seconds., the attention problems interfere with daily life on a significant manner (e.a. driving). Severely abnormal scores (above 25-30 seconds) are a reliable indicator (a warning sign') for underlying organic disorder: MCI and all variants of beginning cognitive impairment (AD, FLD, PDD, LBD e.g.). This clinical finding pushed us to use the test systematically, as vague complaints of headache, vertigo, fear or depression can be the first symptoms of a degenerative process in a population above 65.

Conclusion: 1- The web based CVST is a reliable test for screening attention and memory deficits in first line. Repeating the test over time, gives a consistent and reliable image of the clinical situation and evolution. 2- False positive results are mostly related to anxiety, slowing due to an obsessive behavior, and/or computer-aversion.

Disclosure: Nothing to disclose

EP1005

Complement system dysregulation and quantitative EEG changes in Alzheimer's disease

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Background and aims: Complement dysregulation has been related to Alzheimer's disease (AD) and epileptogenesis. Consistently, it has been demonstrated in animal model studies the role of complement system activation in causing both seizures and neurodegeneration. The aim of the present study is to measure the complement factors in AD patients and correlate their levels with quantitative EEG (qEEG) and CSF AD biomarkers changes.

Methods: Patients affected by AD pathology were compared to patients affected by other neurological disorders (OND). Both AD and OND underwent a protocol including neurological examination, neuropsychological testing, CSF AD biomarkers analysis, EEG, and quantification of serum complement factors concentrations (C3, C4, C1q, CH50, C1inh). In particular, we correlate CSF, serum and clinical data with qEEG analysis selecting the temporal lobe regions (F7, T3, T5, F8, T4, T6). Relative power of EEG bands (delta, theta, alpha and beta) was considered as reference parameter.

Results: We documented the significant reduction of serum C3 levels in AD patients compared to OND ($p < 0.05$). Considering the correlation analysis in the AD group we documented the significant interplay between C1q serum levels and tau/Ab42 ratio ($R = -0.61$) and between C4 and CSF Ab42 concentrations ($R = -0.73$). Moreover, we documented significant correlations between lower C1q serum levels and slowing of EEG. Conversely, the reduction of C3 serum concentrations was related to the reduction of faster EEG rhythms

Conclusion: This pilot study reported that complement system dysregulation may occur in AD pathology and may be related to a more severe neurodegeneration and to the pathological slowing of qEEG.

Disclosure: Nothing to disclose

EP1006

Cancelled

EP1007

Effects of physical exercise on Alzheimer's biomarkers: A systematic review of intervention studies

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Background and aims: Physical exercise may ameliorate symptoms of Alzheimer's disease (AD). Animal studies have suggested this may be mediated through an effect on AD pathology. Therefore, we undertook a systematic review of randomised trials examining effects of physical exercise on validated AD biomarkers.

Methods: Studies eligible for inclusion were intervention studies of physical exercise with 1 or more of the following AD biomarkers as outcome measures: a) A β 1-42, Total-tau and/or Phosphorylated-tau in cerebrospinal fluid; b) 18F-FDG-PET imaging, c) amyloid-PET imaging or d) hippocampal volume measured on MRI in healthy subjects, subjects with subjective cognitive complaints, patients with MCI or AD dementia. Databases searched: MEDLINE, EMBASE, Cochrane Register of Controlled Clinical Trials, PsycInfo and Web of Science.

Results: 54205 citations were identified. Of these 7 papers were included, containing 508 participants (252 in intervention group, 256 in control group) (figure 1). Outcome measure was change in hippocampal volume on MRI and AD biomarkers in CSF. Two studies reported an effect of aerobic exercise on hippocampal volume. One study found an absolute increase in the volume of the anterior hippocampus, which was significant compared to the control group. Another study found a detrimental effect of aerobic exercise in CA2/3 and dentate gyrus/CA4 subregions relative to the control group.

Time-of Examination	Indicators	Group-1	Group-2
		Tempo-rhythmic correction	Control
Initial	Step-Variability-Factor (SVF)	0.51±0.09	0.52±0.06
	Average-Step-Length (ASL)	38.00±6.44	36.2±3.96
In 6 months	Step-Variability-Factor (SVF)	0.27±0.07*	0.40±0.06
	Average-Step-Length (ASL)	46.85±5.89*	38.21±3.73

*-p<0.05 (vs. control)

Figure 1: PRISMA flow chart showing flow of citations in the study

Conclusion: The present findings do not support an effect of physical activity on AD biomarkers and subsequently AD pathology. However, evidence is sparse, and therefore a

possible effect of physical exercise on AD pathology cannot be ruled out. Further studies applying AD biomarkers in rigorously conducted studies are needed.

Disclosure: Nothing to disclose

EP1008

Association of plasma β -amyloid with cognitive performance and decline in chronic kidney disease

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Background and aims: Decreased β -amyloid (A β) clearance from the brain has been suggested to contribute to cerebral A β accumulation in Alzheimer's disease. Based on the idea of a dynamic A β equilibrium in different body compartments, plasma A β levels have been investigated as biomarker candidates for preclinical Alzheimer's pathology, yet with inconsistent results. Since the kidneys are involved in A β elimination from the blood, we evaluated how chronic kidney disease (CKD) affects the association between plasma A β and cognitive deficits and cognitive decline.

Methods: In 28 CKD patients stages 3-5D and 26 control subjects with comparable vascular risk profile from the New Tools for the Prevention of Cardiovascular Disease in Chronic Kidney Disease (NTCVD) cohort, plasma total A β was determined with a highly sensitive electrochemiluminescence-immunoassay. Cognition was evaluated using a comprehensive battery of ten neuropsychological tests at baseline and 2-year follow-up.

Results: Subjects with high plasma A β level (above median) demonstrated a significantly worse baseline cognitive performance than subjects exhibiting low A β level (summary score of global cognitive performance at baseline $z=-0.46\pm0.76$ vs $z=-0.08\pm0.57$, $p=0.045$). Cognitive performance moderately decreased over the 2-year-follow-up in subjects with high plasma A β level ($\Delta z=-0.13\pm0.51$), but increased in subjects with low plasma A β level ($\Delta z=0.16\pm0.41$, $p=0.023$). In linear regression analyses, baseline plasma A β was significantly associated with cognitive decline both in unadjusted analyses ($\beta=-0.28$, 95% CI= -0.55 to -0.01) and analyses adjusted for age ($\beta=-0.27$, 95% CI= -0.54 to -0.01).

Conclusion: Our results suggest the utility of plasma A β level in predicting cognitive decline in patients suffering from CKD.

Disclosure: Nothing to disclose

EP1009

Peripheral neuropathy as clinical onset in E200K familial Creutzfeldt-Jakob disease

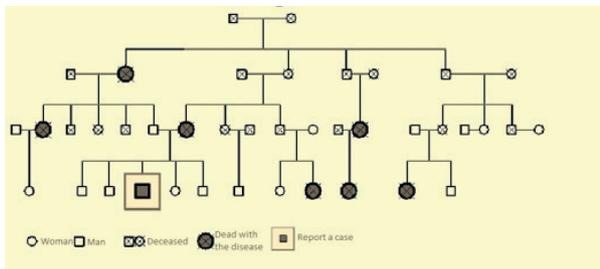
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Background and aims: To report a case of familial Creutzfeldt-Jakob disease (fCJD) with peripheral neuropathy as unusual clinical presentation and a cluster of 8 members with fCJD in Guadalajara, Spain.

Methods: A non-diabetic 65-year-old male presented a history of 6 middle-aged family members, in an autosomal dominant inheritance pattern, who died of neurological diseases, described as rapidly progressive cognitive and gait impairment. Our patient presented with a history of 4 months characterized by unsteady gait, numbness and paresthesias on both feet. Initial examination evidenced mild gait ataxia, generalized osteotendinous hyporeflexia and distal lower extremities vibratory and tactile hypoesthesia. 2-3 months later, he developed progressive and severe gait ataxia, bilateral appendicular dysmetria, "nocturnal jerks", bilateral hypoacusis, slow and hypometric saccades, decreased visual acuity and lately temporospatial disorientation, visual hallucinations and insomnia that persist daily.

Results: Complementary blood tests for potential causes of acquired ataxia and peripheral neuropathy, including onconeural antibodies were negative. 2 cranean MRI showed unspecific brain atrophy, including cerebellum, panmedular MRI was normal and EEG was normal. EMG evidenced a mixed and severe sensory-motor neuropathy. Audiometry exam found a bilateral 50% hearing loss. CSF exam revealed a positive 14-3-3 protein. Genetic testing for PRPN gene evidenced the E200K mutation and a polymorphism in the codon 129 methionine/valine, in heterozygosis.



Family tree

Neurophysiological study: motor, sensory and lower SEP conduction values									
	DML ms	Amp CMAP mV	MCV m/s	Amp CMAPm V	F wave	SCV m/s	Amp CSAP µV	P17 ms	P17 Cort Amp µV
L Cubital	3,66	3,1	-	-	-	53	4	-	-
L Superficial Peroneal	6,88	6,6	48	0,4	-	Absent	Absent	-	-
R Superficial Peroneal	-	-	-	-	-	Absent	Absent	-	-
L Tibial	7,52	2,8	33	1,5	Absent	-	-	56,7	0,52
R Tibial	6,77	4,7	33	1,6	Absent	-	-	52,7	0,6
L Sural	-	-	-	-	-	Absent	Absent	-	-
R Sural	-	-	-	-	-	Absent	Absent	-	-

SEP: Somatosensory evoked potential
DML: Distal motor latency
CMAP: Compound motor action potential
MCV: Motor conduction velocity
SCV: Sensory conduction velocity
CSAP: Compound sensory action potential

Neurophysiological study

Conclusion: An atypical case of familial Creutzfeldt-Jakob disease, presenting with peripheral neuropathy and having delayed central symptoms, is described. A cluster Spanish family with 7 affected members is reported.

Disclosure: Nothing to disclose

EP1010

Cancelled

EP1011

Basal forebrain atrophy is associated with elevated plasmatic homocysteine levels in subjects at risk of Alzheimer's disease

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Background and aims: Increased homocysteine plasmatic level (HPL) is recognized as risk factor for Alzheimer's disease (AD). Basal forebrain (BF) neurons, that are major source of acetylcholine, degenerate early in the course of AD. Recent findings suggest increased HPL lowers the number of BF cholinergic neurons. We aimed to assess the association between HPL, BF and hippocampal volumes in cognitively normal elderly (NC), subjects with subjective cognitive decline (SCD), mild cognitive impairment (MCI) and AD dementia.

Methods: In total 96 subjects; NC (n=11); SCD (n=30); MCI (n=39); AD (n=14) had volumetric brain MRI at 1.5T and blood sampling. Hippocampal and BF volumes were computed using a mask based on cytoarchitectonic map derived from a postmortem brain. MRI scans were time-matched with HPL blood sampling. Analysis of variance and multiple linear regression were used to assess mutual associations.

Results: Elevated HPL was associated with lower BF volumes ($R^2=0.52$; $p=0.016$). Analysis of separate BF nuclei showed associations of HPL with medial septum, vertical limb of diagonal band (DB) ($R^2=0.25$; $p=0.01$), nucleus subputaminalis ($R^2=0.38$; $p=0.04$) and horizontal DB limb ($R^2=0.48$; $p=0.03$). There was no association between HPL and hippocampal volume.

Conclusion: The HPL is associated with BF but not with

hippocampal atrophy. This agrees with animal studies showing that hyperhomocysteinemia is associated with reduction in number of BF cholinergic neurons. Our data suggest that increased HPL may be one of the factors contributing to early degeneration of BF during the course of AD.

Disclosure: This project was supported by the Alzheimer Foundation, AVAST Foundation, Grant FNUSA-ICRC (no. CZ.1.05//1.1.00/ 02.0123) from European regional development fund, Grant Agency of Charles University in Prague Grant No. 624012.

EP1012

Cancelled

EP1013

Hypothalamic dysfunction is related to sleep impairment and CSF biomarkers in Alzheimer's disease

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Background and aims: Hypothalamus is a key brain region affected by the Alzheimer's disease (AD) pathology and regulating several essential homeostatic functions, including the sleep-wake cycle. We investigated the possible in vivo alteration of the hypothalamus and its correlations with sleep impairment and cerebrospinal-fluid (CSF) AD biomarkers changes in a population of AD patients compared to non-demented elderly controls.

Methods: We measured the polysomnographic sleep, the CSF AD biomarkers and orexin levels, and the hypothalamic [18F] FDG PET uptake in a population of AD patients.

Results: We documented the significant reduction of hypothalamic [18F]FDG PET uptake in the AD group (n=18) compared to the Control 2 group (n=18) (p<0.01). Moreover, we found the increase of CSF orexin levels coupled with the marked alteration of the nocturnal sleep in the AD group as compared to the Control 1 group (n=15) (p<0.05). Finally, we observed the significant association linking the reduction of both sleep efficiency and REM sleep to the reduction of hypothalamic [18F]FDG PET uptake in the AD group. Moreover, [18F]FDG PET hypothalamic uptake correlated with the higher ratio of total-tau/beta-amyloid42 CSF levels (index of more marked neurodegeneration). Finally, we documented a connection between the hypothalamus and the limbic system in the control group, which was not evident in the AD group.

Conclusion: In conclusion, we documented the in vivo dysfunction of the hypothalamus in AD patients, which was correlated with both the impairment of nocturnal sleep and the CSF index of more marked AD neurodegeneration.

Disclosure: Nothing to disclose

EP1014

Frequency and risk factors for appetite and eating disturbances in Alzheimer's disease

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Background and aims: Our goal is to evaluate the frequency of appetite/eating disturbances in Alzheimer's disease (AD) and to determine the features associated with its development.

Methods: A cross-sectional study in 173 consecutive patients with probable AD (NIA-AA criteria) followed-up in a Dementia Unit in Spain (mean age at onset 75.2±6.7 years and mean duration of dementia 3.8±2.0 years, 71.7% women, Mini-Mental State Examination 16.7±6.1). The 12th item in Neuropsychiatric Inventory (NPI) was used to assess appetite/eating disturbances.

Results: Overall, appetite/eating disturbances occurred in 44.5% of participants, and in 35.8% were "clinically relevant" [NPI ≥ 4]. These were associated with depression (p=0.042), apathy (p<0.0001), disinhibition (p=0.026), aberrant motor behaviour (p=0.047) and antidepressants use (p=0.013). By domains, 30.6% experienced appetite loss (15% of them coexistent with dysphagia), and it was significantly more prevalent in women, subjects with depression, apathy or antidepressant medication. In contrast, 15.0% presented increase in appetite, change that was more frequent in those individuals with more severe dementia [CDR-3], disinhibition or higher MMSE/year decline. 6.9% had an unusual eating behaviour (e.g. tending to overfill mouth) which was associated with more severe dementia, hallucinations, agitation, multiple drug therapy and rapid progression. Other 6.9% had suffered a change in his/her food preference (e.g. preferring sweet foods more than before) in which a widower status, disinhibition and aberrant motor behaviour were associated factors.

Conclusion: Appetite disturbances are frequent in AD, but risk factors for them differ according to the type of appetite/eating disturbance assessed.

Disclosure: Nothing to disclose

Cerebrovascular diseases 1

EP1015

Cancelled

EP1016

Cancelled

EP1017

Focal cerebral arteriopathy: A well-characterized cause of stroke in pediatric age

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Background and aims: Focal cerebral arteriopathy is an uncommon cause of stroke in pediatric age. This idiopathic clinical syndrome consists of unilateral intracranial arteriopathy involving distal carotid artery and proximal segments of middle and anterior cerebral artery. We present our clinical experience in the management of this entity.

Methods: We present 3 cases of girls with ages between 10 and 16-year-old, admitted to our center with the diagnosis of acute ischemic stroke between 2013 and 2016. Complementary tests including angiography and their evolution, were consistent with the diagnosis of focal cerebral arteriopathy.

Results: At initial evaluation their National Institute of Health Stroke Scale (NIHSS) score was 16 or greater. One patient received intravenous thrombolysis treatment, the other two were beyond the time window. Another patient underwent endovascular treatment 8 hours from stroke onset. In all cases, the angiographic studies showed supraclinoid carotid and ipsilateral proximal middle cerebral artery involvement, which consisted of focal stenosis. Radiological worsening at 6 months was observed in one patient, without clinical relevance. All patients had characteristic lenticulostriate infarction demonstrated on MRI. A complete etiological study was performed, with no additional findings. None presented new ischemic events and all showed a trend for clinical improvement.

Conclusion: Focal cerebral arteriopathy is a typical pediatric disease with a characteristic vascular involvement pattern. It has an overall good prognosis although it is necessary to consider the possibility of radiological worsening.

Disclosure: Nothing to disclose

EP1018

Optimal glucose control may prevent small-artery occlusion subtype of ischemic stroke in patients with type 2 diabetes mellitus

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Background and aims: Although optimal glycemic control is recommended in patients with type 2 diabetes mellitus (DM), whether this can prevent ischemic stroke, remains unclear. Our study investigated whether optimal glycemic control could influence etiologic patho-mechanism of acute stroke in patients with DM.

Methods: We studied acute ischemic stroke patients who were admitted between January 2009 and December 2013 and had been treated with hypoglycemic agents. The controlled group comprised patients with less than glycated hemoglobin level (HbA1c) 7% at admission. The clinical characteristics, laboratory results, antidiabetic drugs, and stroke subtypes (large-artery atherosclerosis, cardioembolism, and small-artery occlusion) were compared between controlled and uncontrolled groups.

Results: Of 259 patients with DM (female 43.7%, mean age 68.5±9.6 years), only 82 patients (31.7%) showed a controlled HbA1c. Small-artery occlusion subtype was most common (43.5%) in uncontrolled group and was the least common (26.8%) in controlled group. The HbA1c showed 7.9% (IQR 7.1–9.2) in small-artery occlusion, 7.4% (IQR 6.8–8.5, p=0.029) in large-artery atherosclerosis, and 7.2% (IQR 6.3–7.8, p=0.001) in cardioembolism. In addition to low density lipoprotein-cholesterol and high density lipoprotein-cholesterol levels, small-artery occlusion subtype was independently associated with HbA1c (odds ratio 1.26; 95% confidence interval 1.05–1.51, p=0.011). However, HbA1c was not associated with large-artery atherosclerosis subtype, and with the class of antidiabetic agents.

Conclusion: In patients with DM, optimal glycemic control may reduce the incidence of the small-artery occlusion subtype of ischemic stroke, not large-artery atherosclerosis subtype.

Disclosure: Nothing to disclose

EP1019

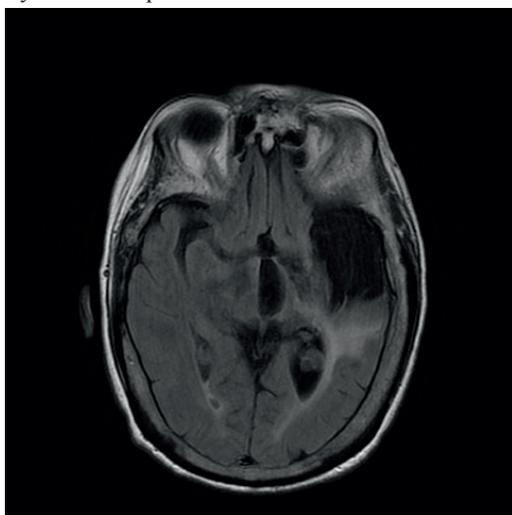
Why are there so many cerebral infarcts in the same hemisphere? Adult presentation of Dyke-Davidoff-Masson Syndrome or acquired hemiatrophy.

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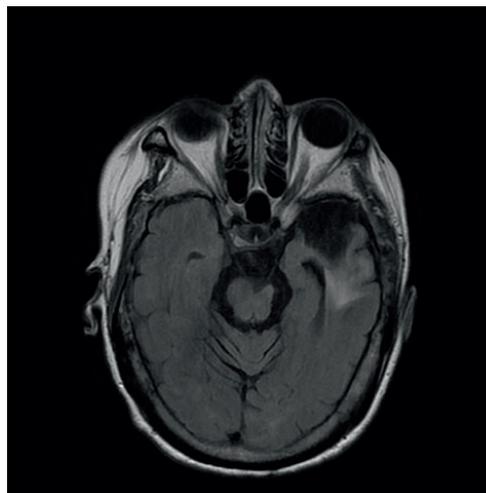
Background and aims: To present a patient with Dyke-Davidoff-Masson syndrome as a rare cause of susceptibility to repetitive ischemic strokes in the same cerebral hemisphere.

Methods: A 62-year-old woman with history of severe mitral valvulopathy associated with atrial fibrillation, partial seizures and recurrent stroke in the left cerebral hemisphere. She had no pre or perinatal complications. However, she had meningoencephalitis with seizures at the age of 28 months. At age 45, she presented a first ischemic event in territory of left posterior cerebral artery that recovered without sequelae, 5 years later she had a ischemic stroke of left middle cerebral artery with mixed aphasia and right hemiplegia that did not improve. 12 years after the first stroke she presented a new infarct of left anterior cerebral artery despite always maintaining therapeutic levels of INR (International Normalized Ratio), dying by respiratory infection during this process.

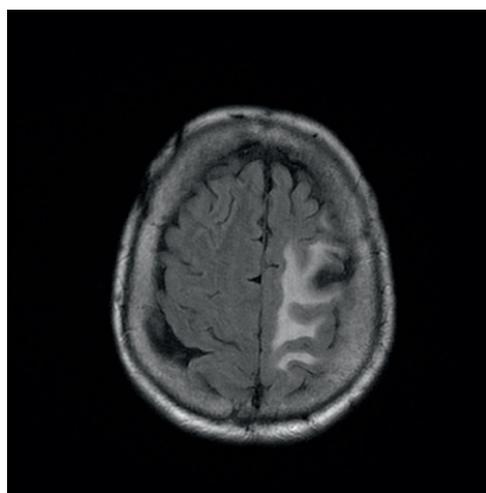
Results: The vascular study to causes of recurrent stroke was normal after extensive study, however, in all the neuroimaging performed, additionally to the areas of malacia corresponding to the previous infarctions, marked atrophy of the left hemisphere was evident, predominantly in the cerebral peduncle, cerebellar hemisphere, thalamus and frontoparietal cortex. Given this clinical context, we established the diagnosis of Dyke-Davidoff-Masson Syndrome acquired.



Left thalamic atrophy.



Left cerebral peduncle atrophy.



Left cortical atrophy.

Conclusion: This case shows a rare form of recurrent ictus in a hemisphere and its identification would allow to generate longitudinal studies to ascertain the natural course of this syndrome especially in an adult population, which would help in planning approaches to the time, nature of interventions and management accordingly.

Disclosure: Nothing to disclose

EP1020

Voluntary control of plegic limb during yawning after stroke

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Background and aims: Stereotyped movements of paretic limbs during yawning in stroke patients are common, although rarely reported. They are described as involuntary actions.

Methods: We present the first report of voluntary control of a plegic superior limb during yawning.

Results: 59-year-old patient, admitted with an acute left middle cerebral artery stroke (NIHSS 12). Endovenous thrombolysis was administered but plegia of the right superior limb persisted. Since the first hours of stroke, the patient presented with a stereotyped movement with flexion of the elbow of the plegic limb while yawning. Remarkably, at day 6, patient started to have voluntary movement control of the plegic limb while yawning. Ability to touch the chin or the left shoulder with the right hand according to the request of the observer was documented by video. MRI showed an ischemic lesion involving lenticular nucleus, anterior and posterior limbs of internal capsule, body of caudate nucleus and corona radiata. We performed an overlay study using two patients with lenticulo-capsulo-radiata lesions as controls. Softwares FSL and MRICron were used. Analysis showed that this patient had more involvement of the anterior, posterior and inferior regions of the putamen, although the difference was not significant. Motor deficit improved to paresis after 30 days. The described phenomenon remained.

Conclusion: To our knowledge this is the first report of voluntary control of a plegic limb during yawning. Lesion overlay studies with more controls can contribute to the identification of a specific lesion pattern underlying this singular phenomenon.

Disclosure: Nothing to disclose

EP1021

Prognostic value of prealbumin in patients with ischemic stroke

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Background and aims: Blood–cerebrospinal fluid barrier (BCSFB) maintains stable and well controlled environment which is essential for the central nervous system functions. The probable link between brain ischemia and capabilities of BCSFB located in choroid plexus has not been extensively explored. Prealbumin (PA) is a protein synthesized in the liver as well as in the choroid plexus. We investigated the possible association between levels of this protein and outcome in ischemic stroke.

Methods: In this prospective observational study 81 patients with acute ischemic stroke consecutively admitted to Stroke Unit were included. The functional status at the day of hospital discharge was evaluated with the modified Rankin Scale (mRS) and the patients were classified into two groups: unfavorable (mRS score ≥ 3) and good (mRS score < 3) outcome. In multivariate analysis we assessed the relations of PA levels with the unfavorable outcome. One-year mortality was analyzed by Kaplan–Meier survival curves stratified by mean value of PA.

Results: Compared with patients with mRS < 3 , patients with an unfavorable outcome at hospital discharge had significantly lower PA levels ($P < 0.0001$). In multivariate analysis, PA was an independent predictor for unfavorable outcome at the day of hospital discharge (adjusted odds ratio = 0.96; 95% CI: 0.9–0.99, $P < 0.05$). Patients with lower PA concentration had a higher risk for death, in contrast with patients in whom PA levels exceeded mean value = 46.9 mg/dl ($p = 0.02$).

Conclusion: The serum PA level status is associated with the functional outcome in patients with acute ischemic stroke. It could be useful factor in stroke outcome prognosis.

Disclosure: Nothing to disclose

EP1022

Cerebrovascular disease in a Sicilian elderly community: Results from a population based study

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Background and aims: Stroke is one of the most disabling and burdensome health conditions worldwide. Our aim was to assess incidence and mortality rates of cerebrovascular disease, in a Sicilian population using data from a population-based survey of elderly participants.

Methods: A door-to-door survey was carried out in the city of Bagheria, Sicily (prevalence day September 30th, 2006). A cohort of 2,200 persons was randomly stratified, obtaining a 25% sample of the whole population aged 65 years or more. We obtained clinical data for the whole cohort after nine year from local Health Institution. Individuals were evaluated at baseline (2007-2008) and at the end of follow-up period (2016). We calculated crude, and age and sex specific incidence rates, as well as cause specific mortality rates, with 95% confidence intervals.

Results: We identified 176 incident patients with cerebrovascular disease during the follow up giving a total incidence of 888.9/100,000 person years (CI: 888.86-888.94). Incidence rate was higher in men (1010.00, CI: 1009.94-1010.06) than women (790.30; CI: 790.24-790.36). Cause specific mortality rate for CVD was 353.54/100,000 (CI: 353.50-353.58) in the whole cohort, 420.12 in men (CI: 420.06-420.18) and 297.54 in women (CI: 297.48-297.60). Age-specific incidence rates of cerebrovascular disease increased with advancing age.

Conclusion: In the Bagheria Cohort study, incidence of cerebrovascular diseases increased with age. Stroke incidence rates and mortality were significantly higher for men compared to women. Our incidence rates provide new estimates for projection of future burden of disease in Italy and should be considered when planning prevention and stroke care services in this region.

Disclosure: Nothing to disclose

EP1023

ECG changes and its effect on prognosis in acute ischemic stroke patients without cardiac pathology

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Background and aims: Acute ischemic stroke has effect on ECG results and cardiac enzyme levels, but its mechanism has not been clearly established. Our aim in this study is to research ECG and cardiac enzyme changes in acute ischemic stroke and to investigate association between these changes and stroke localization, infarct volume.

Methods: The study included 241 acute ischemic stroke patients. Patients with any cardiac pathology and stroke history were excluded. Only patients with normal echocardiography results were included. The risk factors for stroke, CK-MB and TnI levels were recorded. The infarct sizes, localizations and volumes were analysed in MR images. In addition NIHSS scores were noted at application and discharge. ECG results (QTc interval, PR interval, QRS duration, RR interval, ST depression) were measured by a cardiologist. Bazett's formula was utilized to analyse ECG results and abnormality.

Results: 123 patients were with right hemisphere infarcts (mean age: 68.07±11.37 years) and 118 patients were with left hemisphere infarcts (mean age: 68.20±12.59). HT was more common in right hemisphere infarcts (p=0.013). The most common ECG abnormality was QTc extension (31%). TnI levels were higher in 42 patients. CK-MB and TnI levels were significantly higher in patients with right hemispheric infarcts (p<0.05) and TnI levels were also higher in cerebellar infarcts (p=0.008). NIHSS scores and infarct volumes were higher in left hemisphere and cerebellar infarcts (p<0.05).

Conclusion: The most common ECG abnormality was QTc extension. Right hemisphere and cerebellar infarcts may induce ECG changes and increase cardiac enzymes more often.

Disclosure: Nothing to disclose

EP1024

Rheological properties of blood in different subtypes of acute ischemic stroke

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Background and aims: Despite of the diversity and heterogeneity of clinical manifestations of ischemic cerebrovascular diseases, there are universal pathogenetic mechanisms underlying stroke. Blood rheology has extremely important role in vascularisation of the brain: disturbances in hemorheological parameters provoke the development of zone of ischemia, local stasis, hypoxia.

Methods: The study included 94 patients with acute ischemic stroke (age 62 [53;69] years). Subtypes of stroke were indentified according to criteria TOAST (Figure 1). Rheological properties were assessed: blood viscosity, plasma viscosity, fibrinogen concentration, hematocrit, red blood cell aggregation and deformability. The data is presented in the form of Me [Q1; Q3], Me - median, Q1 and Q3 - the lower and upper quartiles. For statistical analysis was been used χ^2 Pearson criterion. The critical level of significance was $p < 0,05$.

Results: Analysis of blood viscosity in all of shear rates had not showed statistically significant differences between groups with different subtypes of stroke (Figure 2). Statistical analysis of plasma viscosity(PV),hematocrit (Ht), deformability in different shear rate (D 90-890), red blood cell aggregation (T1/2) and fibrinogen concentration (Fb) had not showed statistically significant differences between groups with different subtypes of stroke (Figure 3).

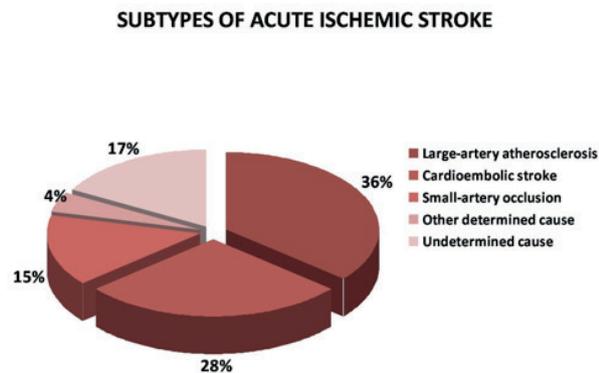


Figure 1. Subtypes of acute ischemic stroke (TOAST criteria)

Stroke subtype	Large-artery atherosclerosis	Cardioembolic stroke	Small-artery occlusion	Undetermined cause	p, χ^2
vk_3	13,4 [11,9;14,6]	12,2 [10,0;14,1]	13,4 [12,8;16,4]	13,3 [10,4;16,5]	$p=0,398, \chi^2=5,1$
vk_5	10,9 [9,9;12,1]	9,9 [8,4;11,8]	10,9 [10,0;12,3]	10,8 [9,0;12,6]	$p=0,439, \chi^2=4,8$
vk_7	10,0 [8,9;10,8]	8,3 [7,7;10,5]	9,8 [8,9;10,6]	9,4 [8,8;10,9]	$p=0,748, \chi^2=2,7$
vk_10	8,9 [8,2;10,0]	7,5 [7,3;9,9]	9,0 [7,7;9,4]	8,4 [7,0;9,7]	$p=0,670, \chi^2=3,2$
vk_50	6,0 [5,8;6,7]	5,5 [5,2;6,6]	6,4 [5,4;6,5]	5,9 [5,0;6,6]	$p=0,676, \chi^2=3,2$
vk_100	5,3 [5,2;6,0]	5,1 [4,7;5,7]	5,8 [4,9;6,0]	5,4 [4,6;6,0]	$p=0,615, \chi^2=3,6$
vk_300	5,0 [4,7;5,4]	4,7 [4,5;5,1]	5,3 [4,6;5,5]	5,0 [4,4;5,5]	$p=0,568, \chi^2=3,9$

Figure 2. Blood viscosity with different subtypes of ischemic stroke (in shear rate 3-300 s-1)

Stroke subtype	Large-artery atherosclerosis	Cardioembolic stroke	Small-artery occlusion	Undetermined cause	p, χ^2
PV	1,6 [1,6;1,7]	1,6 [1,6;1,7]	1,7 [1,7;1,8]	1,7 [1,6;1,8]	$p=0,797, \chi^2=2,4$
Ht	43,6 [40,3;47,0]	41,4 [39,5;45,0]	44,4 [42,1;47,9]	40,6 [38,9;41,8]	$p=0,666, \chi^2=3,2$
D_90	0,190 [0,159;0,210]	0,157 [0,121;0,204]	0,190 [0,186;0,214]	0,195 [0,179;0,222]	$p=0,368, \chi^2=5,4$
D_180	0,212 [0,189;0,297]	0,208 [0,173;0,249]	0,211 [0,203;0,240]	0,260 [0,238;0,271]	$p=0,471, \chi^2=4,6$
D_360	0,297 [0,263;0,340]	0,262 [0,232;0,279]	0,263 [0,247;0,293]	0,299 [0,247;0,349]	$p=0,439, \chi^2=4,8$
D_890	0,365 [0,329;0,394]	0,320 [0,278;0,334]	0,388 [0,311;0,396]	0,375 [0,311;0,381]	$p=0,217, \chi^2=7,0$
T _{1/2}	4,6 [3,5;6,6]	4,1 [2,0;6,2]	3,3 [3,0;3,9]	2,9 [2,2;6,5]	$p=0,906, \chi^2=1,6$
Fb	3,7 [3,2;4,0]	3,3 [3,1;3,5]	3,3 [2,9;3,6]	3,1 [2,9;3,7]	$p=0,530, \chi^2=3,6$

Figure 3. Rheological properties with different subtypes of ischemic stroke

Conclusion: The lack of significant differences in rheological parameters at different subtypes of ischemic stroke shows that the change in blood rheology is a universal pathophysiological mechanism of acute cerebral ischemia.

Disclosure: Nothing to disclose

EP1025

Blood viscosity in acute ischemic stroke

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Background and aims: Important role in the pathogenesis of ischemic stroke belongs hemorheological properties, leading to diffuse and focal changes in the brain tissue. Blood viscosity (BV) is one of the main rheological parameters, what is measuring the resistance of blood to flow. The aim of study is evaluation of BV at ischemic stroke in dynamic within 20 days after onset.

Methods: The study included 94 patients with acute ischemic stroke (IS) (age 62 [53;69] years) and 20 control patients, age 55 [54;59]. BV was assessed by rotational viscometry at shear rates 3-300 s⁻¹. BV was been measured in the first 12 hours, in 3-5 and 18 - 20 days of stroke. The data is presented in Me [Q1; Q3]. For statistical analysis was been used nonparametric Mann-Whitney U-test. The critical level was p<0.05.

Results: Patients in the first 12 hours after IS had significant changes in BV in all shear rates compared with control group (Table 1, Figure 1). Patients in 3-5 days after IS had significant changes in blood viscosity: 38% in shear rate 3 s⁻¹ (p=0.002, U=203), 35% in 5 s⁻¹ (p=0.003, U=205), 27% in 7 s⁻¹ (p=0.011, U=232), 19% in 10 s⁻¹ (p=0.03, U=257). In 18-20 days after IS patients had difference in BV for 24% in 3 s⁻¹ (p=0.023, U=175) and 19% 5 s⁻¹ (p=0.03, U=181).

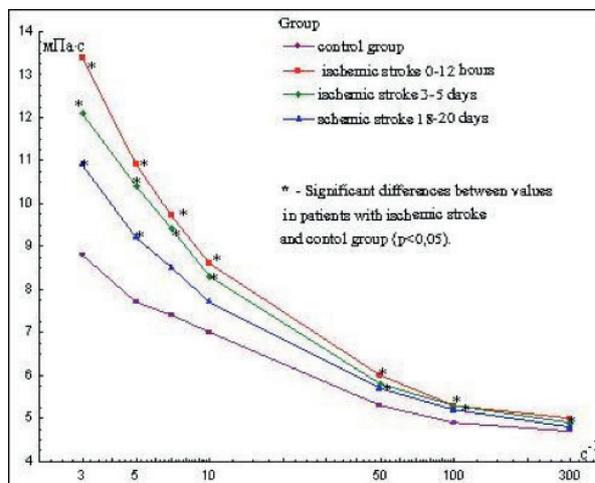


Figure 1. Blood viscosity at different shear rates in patients with ischemic stroke in dynamic within 20 days after onset

Conclusion: We found long-term preservation of increased blood viscosity at low shear rates in ischemic stroke. Hyperviscosity syndrome is the important pathogenetic mechanism at the level of microcirculation in patients with acute cerebral ischemia.

Disclosure: Nothing to disclose

	Ischemic stroke, n=94			Control group, n=20
	0-12 hours	3-5 days	18-20 days	
3 s ⁻¹	13,4 [10,4;15,2] *	12,1 [9,5;16,3] *	10,9 [10,2;13,6] *	8,8 [8,0;12,5]
5 s ⁻¹	10,9 [9,0;12,2] *	10,4 [8,1;12,0] *	9,2 [8,5;10,7] *	7,7 [6,4;10,4]
7 s ⁻¹	9,7 [8,3;10,8] *	9,4 [7,5;10,2] *	8,5 [7,5;9,7]	7,4 [5,9;9,3]
10 s ⁻¹	8,6 [7,4;9,9] *	8,3 [6,7;9,1] *	7,7 [6,8;8,8]	7,0 [5,7;8,2]
50 s ⁻¹	6,0 [5,4;6,6] *	5,8 [5,2;6,3]	5,7 [5,2;6,7]	5,3 [4,8;5,9]
100 s ⁻¹	5,3 [4,9;6,0] *	5,3 [4,8;5,6]	5,2 [4,7;5,8]	4,9 [4,5;5,3]
300 s ⁻¹	5,0 [4,5;5,5] *	4,9 [4,4;5,2]	4,8 [4,4;5,4]	4,7 [4,3;4,9]

Table 1. Blood viscosity in patients with ischemic stroke and control group (* – significant differences between values in patients with ischemic stroke and control group)

EP1026

Cancelled

EP1027

Recurrent intracerebral hemorrhage in young age – can traumatic brain injury induce cerebral amyloid angiopathy?

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Background and aims: Cerebral amyloid angiopathy (CAA) by deposition of amyloid- β protein (A β) characteristically occurs sporadically in persons aged ≥ 55 years. Some rare familiar forms can occur at younger ages. We report the case of a young woman with recurrent cerebral hemorrhages with pathological evidence of amyloid- β angiopathy

Results: 33-year-old female, with past history of traumatic brain injury at the age of 1 year with right parietal fracture, requiring cranioplasty at ages of 3,7,8 years, was admitted with sudden onset of left hemiparesis and sensory loss. CT scan showed a right fronto-parietal hematoma. Etiologic investigation, including Digital Subtraction Angiography (DSA), was negative. Six years later, she was readmitted with headache. CT scan showed a lobar hemorrhage in the left frontal lobe. Repeated DSA was normal, lumbar puncture showed low levels of β -amyloid protein. Cerebral biopsy showed severe CAA, with extensive capillary involvement, with scarce amyloid plaques and without tau-pathology or associated-inflammation. Genotyping of APP gene was negative and apolipoprotein-E showed heterozygosity for ApoE4. In the next months she suffered multiple spontaneous cortical hematomas and she died two months after the last admission.

Conclusion: At younger ages CAA is a rare disease and is normally associated with genetic disease. In our case, the previous history of traumatic brain history cannot be ignore and although its role is not clear, evidence has accumulated about the possible association between traumatic brain injury and CAA particularly at younger ages.

Disclosure: Nothing to disclose

Cerebrovascular diseases 2

EP1028

Cancelled

EP1029

On the role of Na⁺ in controlling cerebrospinal fluid (CSF) osmolality

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Background and aims: Osmolality plays a relevant role in controlling neuronal cell volume as well as swelling or shrinking under ipo- and iper-osmolality status. Na⁺ is the major, although the non exclusive, determinant of both CSF and serum osmolality. Serum and CSF osmolalities are in equilibrium due to the equilibrium of major osmolites across the blood-brain barrier. The present study was planned in order to investigate the possibility that CSF Na⁺ could play an independent role in controlling CSF osmolality

Methods: CSF and sera from 60 patients were employed in this study. Na⁺, glucose, nitrogen urea were measured using Siemens ADVIA 1800 Chemistry. Osmolality was measured directly or calculated using three different algorithms employing the concentrations of Na⁺, glucose and urea nitrogen. The osmolality gap was calculated by subtracting the calculated to the measured values.

Table I: computational algorithms employed to calculate serum or CSF osmolality

Algorithms	Formulae
Alg 1	Osmolality = (2*Na ⁺) + (glucose/18) + (urea nitrogen/2.8)
Alg 2	Osmolality = (1.86*Na ⁺) + (glucose/18) + (urea nitrogen/2.8) + 9
Alg 3	Osmolality = ((1.86*Na ⁺) + (glucose/18) + (urea nitrogen/2.8)) * 1.09

Table I

Results: CSF and serum Na⁺ concentrations were correlated although, in approximately 25% of cases (all characterized by a moderate hyponatremia,) CSF Na⁺ was definitely higher than serum Na⁺. Despite these differences, CSF and serum osmolalities were superimposable and correlated. The CSF-serum Na⁺ difference was (a) inversely related to serum (but not CSF) Na⁺ concentration, (b) directly correlated with serum (but not CSF) osmolality gaps, (c) inversely correlated with the CSF-serum osmolality gap difference, (d) directly correlated with serum (but not CSF) Na⁺-independent osmolality and (e) directly correlated with CSF-serum Na⁺-independent osmolality.

Table II: Differentiation of Na⁺ S, Osmolality gap, Difference (CSF-S) in osmolality gap, Na⁺-independent osmolality serum and difference (CSF-serum) of Na⁺-independent osmolality according to quartiles of difference in CSF-serum Na⁺ concentration

Quartiles of CSF-S difference in Na ⁺	Difference (CSF-S) in Na ⁺ , mEq/L	Na ⁺ S, mEq/L	Osmolality gap (alg 1) S, mOsm/Kg	Difference (CSF-S) in osmolality gap (alg 1), mOsm/Kg	Na ⁺ -independent osmolality serum, mOsm/Kg	Difference (CSF-serum) of Na ⁺ -independent osmolality mOsm/Kg
Quartile 1	-0,87 ± 0,91	142,8±2,1	-8,55 ± 4,67	5,95 ± 4,31	2,60±5,17	3,87±4,58
Quartile 2	1,67 ± 0,62	137,8±3,5	-2,92 ± 5,49	2,68 ± 5,46	9,33±6,51	-0,47±5,75
Quartile 3	4,12 ± 1,15	138,3±3,1	-0,81 ± 5,14	0,01 ± 4,75	11,00±4,90	-2,31±4,91
Quartile 4	8,07 ± 1,62	134,9±4,5	4,55 ± 4,65	-4,83 ± 5,98	17,47±6,15	-7,27±6,51

Table II

Conclusion: these data suggest that CSF Na⁺ plays a specific role in controlling CSF osmolality in cases of moderate normoosmolal hyponatremia.

Disclosure: Nothing to disclose

EP1030

Nutritional status measurement using body mass index, waist-to-hip ratio and waist circumference to predict stroke outcome in both genders

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Background and aims: We investigated whether increased waist-to hip ratio (WHC), waist circumference (WC) or improper body mass index (BMI) may differently predict short-term outcome in females and males with first-ever ischemic stroke.

Methods: We retrospectively analyzed data collected in a detailed registry regarding consecutive patients (1109 females and 939 males) admitted due to first-ever ischaemic stroke between 2003 and 2015. BMI 18.5-24.9 kg/m² and gender specific normal values of WHC and WC were used as references for comparisons. Logistic regression was used to calculate odds of in-hospital death or death or dependency at discharge, adjusted for patients' age and prestroke disability.

Results: In both sexes high WHR increased the odds of death or dependency at discharge (OR:1.8, 95%CI:1.05-3.08 for females and 1.43, 95%CI:1.00-2.04 for males), but not in-hospital death alone. Increased WC was significantly associated with lower odds of death or death and dependency at discharge in females only (OR:0.36, 95%CI:0.22-0.58 and 0.69, 95%CI:0.48-0.97, respectively). BMI had no clear predictive value in neither sex.

Conclusion: Among evaluated measure methods only increased WHR was a predictor of poor outcome in both genders, but more significant in females. Abdominal obesity, measured with abnormal WC, was a strong predictor of good outcome in women, but not in men. BMI seemed to have the least clinical value in predicting stroke outcome in both gender.

Disclosure: Nothing to disclose

EP1031

Acid sphingomyelinase inhibitor amitriptyline induces angiogenesis of cerebral microvascular cells by mechanisms involving the Notch pathway

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Background and aims: Post-stroke, new microvessels are formed in the peri-infarct brain, which via release of trophic factors contribute to the remodeling of the brain parenchyma. Strong efforts are currently made in the stroke field to promote neurological recovery by enhancing brain remodeling.

Methods: Following in-vivo observations that the acid sphingomyelinase (ASM) inhibitor and anti-depressant amitriptyline promotes post-stroke angiogenesis, we herein evaluated effects of amitriptyline on the proliferation, migration and tube formation of cerebral microvascular HCMEC/ D3 cells in cell culture. HCMEC/ D3 cells were seeded in proliferation, migration and tube formation assays and treated with various concentrations of amitriptyline.

Results: Amitriptyline dose-dependently increased the migration and tube formation of cerebral microvascular HCMEC/ D3 cells when administered at doses of 5-50 mg/ml, at the same time reducing the proliferation of HCMEC/ D3 cells. These effects were attenuated by N-[N-(3,5-difluorophenacetyl)-L-alanyl]-S-phenylglycine t-butyl ester (DAPT), an inhibitor of Notch signaling pathway.

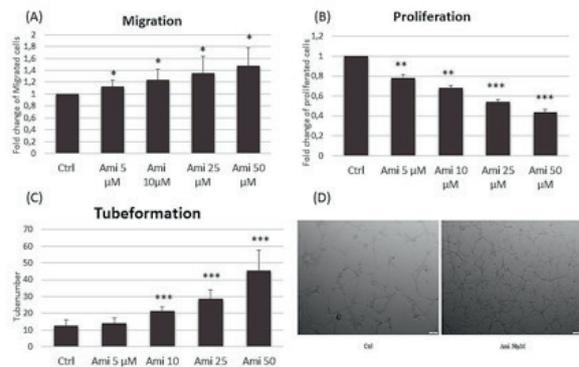


Figure 1: quantification of tube formation (A), migration (B) or proliferation (C) in human cerebral microvascular endothelial cell line (hCMEC/D3) treated with increasing concentrations of amitriptyline; (D) representative pictures showing increased tube formation with 50 µM amitriptyline treatment, scale bar represents 200 µm.

Conclusion: Our data suggest that DLL-4/ Notch signaling is involved in the angiogenic actions of amitriptyline.

Disclosure: Nothing to disclose

EP1032

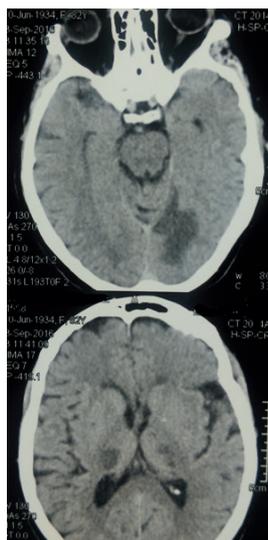
Floating thrombi complicating aortic arch atherosclerosis – probably an under diagnosed cause for embolic stroke

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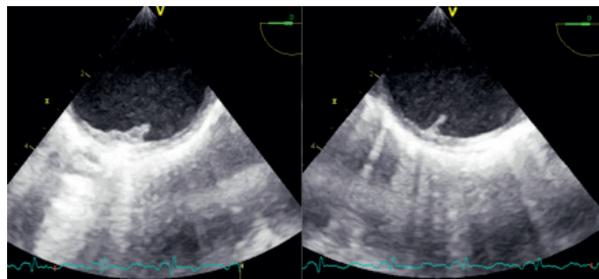
Background and aims: It is viewed that the most frequent causes of ischemic stroke are cardioembolism with atrial fibrillation or atherosclerosis of the cervico-cerebral vessels. However, in up to a third of cases none are present and this is when, among others, an aortic embolic source should be taken into consideration.

Methods: An 82-year-old woman with no prior medical history, was admitted for sudden loss of consciousness. Upon arrival at the hospital she was disoriented, aphasic, tetraparetic, with choreoathetosis of the right arm, head and eyes deviated toward the left. The initial head Computer Tomography (CT) showed no lesions but upon repeating it the next day, there were left occipito-parahippocampal, bilateral thalamic and left cerebellar hypointensities consistent with multiple acute ischemic strokes. Cervical vessel ultrasound and angio CT showed no severe atheromatosis and 24 hour electrocardiographic monitoring was normal. Blood cultures were negative and transthoracic echocardiography was not suggestive of endocarditis.

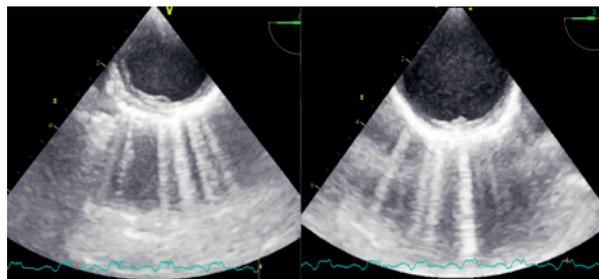


Occipital and bilateral thalamic hypodensities consistent with acute strokes

Results: Transesophageal echocardiography revealed extensive atherosclerotic plaques of the aortic arch, complicated with superimposed floating thrombi. Corroborating all the information we concluded that the most likely source of the stroke was embolism originating at the aortic arch. We decided on double antiplatelet therapy and high dose statin, with very good clinical evolution and significant reduction of the thrombi at two weeks.



Transesophageal echocardiography showing floating thrombi in the aorta



Reexamination after two weeks of double antiplatelet therapy and high dose statin - significant reduction of the aortic plaques and thrombi

Conclusion: Aortic emboli should be considered in stroke patients with no obvious cardioembolic source or significant cervical vessel atherosclerosis. Transthoracic echocardiography is a reliable diagnostic tool. Although reports are scarce, data points towards double antiplatelet therapy as being the treatment of choice.

Disclosure: Nothing to disclose

EP1033

Prehospital stroke scale (FAST PLUS TEST) predicts patients with large arterial vessel intracranial occlusion

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Background and aims: Mechanical thrombectomy is indicated for the treatment of occlusions of large cerebral arteries (LVO), it should be provided as quickly as possible, therefore, a test identifying the suspected occlusion in the pre-hospitalisation stage is needed for the patients to be directed to the centre providing mechanical recanalisation. We assume that the patients with clinically severe hemiparesis have a high probability of the presence of large cerebral vessel occlusion. Therefore, the FAST test was modified to the FAST PLUS test. The FAST PLUS has two parts: the first is the well-known FAST test, the second part evaluates only the presence of severe arm or leg motor deficit (scored 0-1) and unilateral occurrence of its motor function deficit (scored 0-1). Prospective multicenter study to determine specificity and sensitivity of the FAST PLUS test regarding the occlusion of major arteries in the anterior cerebral circulation confirmed by CT angiography (CTA).

Methods: Firstly, paramedics trained in conducting the FAST PLUS test via e-learning. Secondly, in all patients, demographic, NIHSS score, brain CT and CTA were recorded. Sensitivity and specificity of the FAST PLUS test were calculated.

Results: During 10 months 2016, 371 patients were enrolled to study. In 125 patients (33%) CT angiography showed the occlusion of intracranial artery. The sensitivity of the test for ICA/MCA occlusion was 93% and specificity 49%, NPV 93%, PPV 48%.

Conclusion: We found high sensitivity of the FAST PLUS test in our work. The test is suitable for prehospital selection of acute patients with suspected ischemic stroke due to LVO.

Disclosure: Nothing to disclose

EP1034

Cerebral amyloid angiopathy - clinical impact of using the modified Boston criteria

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Background and aims: Early identification of patients with cerebral amyloid angiopathy (CAA) is relevant considering the increased risk for cerebral hemorrhage and the frequent use of antithrombotic therapy. A new set of diagnostic criteria for CAA was recently proposed, which include the presence of superficial siderosis. We aimed to assess the impact of applying these criteria regarding use of antithrombotic therapy.

Methods: We reviewed clinical records of consecutive patients admitted to a Neurology Department from 2014 to 2016, with a possible or probable CAA according to the original and modified Boston criteria. Information was collected regarding presentation, imaging findings and concomitant therapy.

Results: Using the modified Boston criteria, 8 patients fulfilled criteria for probable CAA and 14 for possible CAA. When we applied the original Boston criteria to the same patients, only 7 fulfilled criteria for probable CAA and 8 for possible CAA. Among the additional patients identified with the modified Boston criteria, 4 were using antithrombotic therapy.

Conclusion: The use of the modified Boston criteria allowed for the identification of 7 additional patients, more than half of which were taking antithrombotic therapy. Systematic utilization of these criteria could have an important impact in clinical practice. Raising awareness on the different presentations of CAA among clinicians is of the utmost importance.

Disclosure: Nothing to disclose

EP1035

Risk factors for brain vessels' stenosis in young patients with ischemic stroke

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Background and aims: Thrombophilia is defined as a predisposition to form blood clots and is characterized by deficiencies and mutations in endogenous anticoagulants. Thrombophilic polymorphism such as factor VLeiden, MTHFR mutation (A1298C, C677T), prothrombin mutation G20210A, PAI-1 mutation, antiphospholipid antibodies, Protein S, Protein C are established risk factors for venous thrombosis, but their role in arterial thrombosis is still controversial.

Methods: We investigated prospectively genetic and acquired risk factors for carotid or vertebral stenosis of 49 young patients (age 18-50 years) with ischemic stroke (32 male, 17 female), 18 in vertebrobasilar system, 31 in carotid system. According to stenosis grade patients were divided in two groups - non clinically significant <50% stenosis and clinically significant >50% stenosis/thrombosis. All patients underwent ECG, clinical cardiological evaluation, colour-coded duplex ultrasonography of the cerebral vessels, computed tomography or magnetic resonance imaging of the head and thrombophilia factors examination.

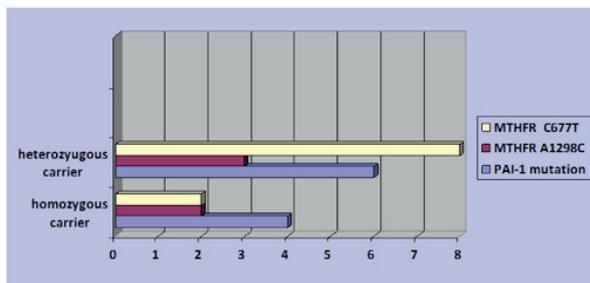


Figure 1 Frequency of thrombophilia in patients with brain vessels thrombosis

Results: The prevalence of acquired risk factors for stroke (arterial hypertension, dyslipidemia, diabetes mellitus, atrial fibrillation, obstructive sleep apnea, smoking, oral contraceptives, family history) are significantly higher in ischemic stroke patients with non clinically significant stenosis. Eleven patients are with thrombosis (5 intracranial and 6 extracranial) and one with severe extracranial stenoses. Ten of these patients have more than one risk factor for thrombophilia plus dyslipidemia. Two patients are only with thrombophilia. The other 37 patients are with ischemic stroke without clinically significant stenosis or thrombosis. Acquired risk factors and hyperhomocysteinemia present in 34 of these patients.

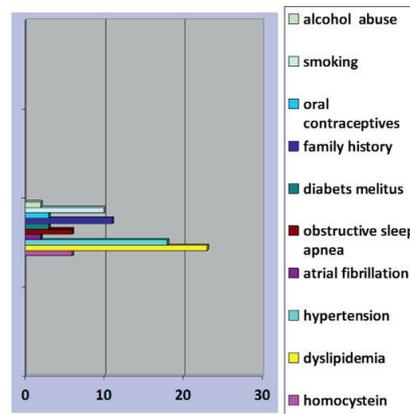
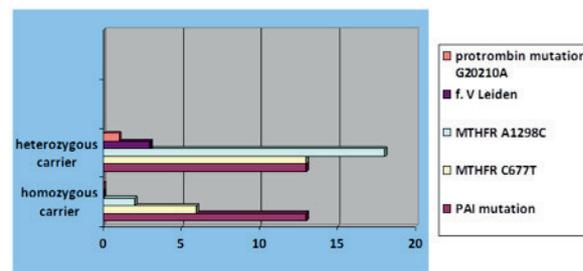


Figure 2 Acquired risk factors

Conclusion: We found that thrombophilia could be a risk factor for severe stenosis or thrombosis in young patients with stroke.



Thrombophilic risk factors in patients without thrombosis

Disclosure: Nothing to disclose

EP1036

Mitochondrial encephalopathy with lactic acidosis and stroke-like episodes (MELAS): A diagnostic challenge

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Background and aims: Mitochondrial encephalopathy with lactic acidosis and stroke-like episodes (MELAS) is a complicated, multi-systemic disorder, known to affect predominantly the brain and skeletal muscles. The early non-specific physical signs, such as short stature, headaches and hypoacusis do not draw sufficient attention until a stroke-like event occurs.

Methods: Case report.

Results: A 19-year-old male presented in our emergency department complaining of numbness and weakness of the left upper limb of abrupt onset. The CT scan revealed an area of hypointensity in the right temporoparietal territory, consistent with an ischemic stroke. On the ward, he experienced a partial seizure. According to his past medical history, he had been thoroughly investigated because of short stature, mild hearing loss, premature adrenarache and features of acromegaly, without reaching a definite diagnosis. He had also received human growth hormone replacement. Karyotype, serum/urine amino acids, as well as enzymes were documented normal. Extensive workout was negative and the stroke was considered of unknown etiology. Four months later the patient experienced an episode of expressive aphasia. Obtaining the family history in detail, we noted that hearing loss and atypical headaches affected at least two generations from the maternal side. That raised suspicion for MELAS, and despite the previously recorded normal electromyography and twice tested normal lactic acid titer, the pathogenic variant m.3243A>G in MT-TL1 was eventually detected in mitochondrial analysis.

Conclusion: MELAS is a diagnostic challenge, worth considering in young patients with vascular incident of unknown etiology. Family history might aid to reach the correct diagnosis.

Disclosure: Nothing to disclose

EP1037

Cancelled

EP1038

Non-traumatic subarachnoid haemorrhage in Malta – are outcomes adversely affected due to lack of a local neurovascular service?

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Objective: The aim of this study was to measure the incidence, treatment and outcome of non-traumatic Subarachnoid Haemorrhage (SAH) cases occurring in Malta during the five-year period between January 2011 and December 2015, in order to determine whether the lack of a local neurovascular service is associated with a poor outcome.

Methods: A retrospective analysis of adult patients (above the age of 16) diagnosed with non-traumatic SAH was carried out. The data collected included a five-year period from January 1st 2011 till December 31st 2015.

Results: The incidence of SAH was estimated at 4.00 cases per 100,000 population per year. An underlying aneurysm was found to be the cause of the SAH in 57.1% of cases investigated with CT angiography or Cerebral Angiography. In these patients, definitive management in the form of coiling or clipping of the aneurysm was carried out in the United Kingdom as part of an agreement between countries, within days. The outcome of these patients measured at 6 months using the Modified Rankin Scale was found to be excellent

Conclusion: Despite our geographical and logistical limitations, outcomes of those patients with initial low Hunt and Hess scores have not been affected by the lack of a local neurovascular service. Results are comparable to those of other international centres. Further studies looking into feasibility of expanding our local services are being carried out

Disclosure: Nothing to disclose

EP1039

Risk factors in young cryptogenic ischemic stroke patients: Findings from the history study

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Background and aims: The cause of ischemic stroke (IS) remains often unclear – cryptogenic, especially in younger patients. Moreover, the presence of known relevant risk factors (RF) is not enough established in this population. Our aim was to assess frequency and spectrum of relevant RF in young CIS patients.

Methods: The study set consisted of young acute IS patients <50 years enrolled in the prospective HISTORY (Heart and Ischemic STrOke Relationship studY) study registered on ClinicalTrials.gov (NCT01541163). In all patients, the brain ischemia was confirmed on CT or MRI. Admission ECG, serum specific cardiac and thrombophilia markers, neurosonology, TEE, 24-hour and 3-week ECG-Holter were performed in all patients to assess CIS.

Results: Out of 1006 patients enrolled in the HISTORY study, 176 (95 males, mean age 40.3 years±8.4 years) were <50 years. 130 (74%) were identified as CIS (72 males, mean age 40.9±7.8 years). In total, relevant RF were present in 88% of CIS patients; 36% of patients had elevated serum cholesterol, 32% of patients were smokers, 30% had detected PFO with right-left shunt, and 28% arterial hypertension. 43% of CIS females used hormonal contraception. Recurrent IS occurred in 5% of CIS patients and all of them had at least one of known RF.

Conclusion: The relevant RF were present in 88% of young CIS patients, hypercholesterolemia and hormonal contraception in females were the most frequent RF.

Disclosure: Study supported by the IGA LF UP_010_2017 and by RVO FNOL 00098892_2017

EP1040

Cancelled

Cognitive neurology/neuropsychology 1

EP1041

Somatoform disorders in neurology

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Background and aims: Functional or medically unexplained symptoms are very common in neurological consultation. In the DSM-IV, these disorders are classified as somatoform disorders. They represent about 30% of the activity of liberal neurologists.

Methods: We report 35 cases of somatoform disorders hospitalized in our general neurology unit over a period of 6 years between 2011 and 2016. The ages ranged from 15 to 80 years. They were 29 women (87.8% of cases).

Results: Psychogenic headaches were the most frequent presenting conditions (42.4%), followed by motor deficits (39.3%), lethargic states (12.1%), ocular symptoms (12.1%), pain (9%), movement disorders (9%), sensory disturbances (6%) and psychogenic nonepileptic seizures (6%). Ten patients exhibited 2 symptoms or more. Anxiodepressive comorbidity was noted in 15% of cases. Eighteen percent of cases had similar episodes in the past. Most of the patients were treated by antidepressants, mainly Amitryptiline, even in the absence of depression. Physiotherapy was used whenever necessary. The evolution was favorable in 57.5% with full recovery before discharge in 42.4%.

Conclusion: 50% of the patients with somatoform disorders are identified by neurologists. The neurologist is faced with the challenge of asserting the diagnosis and making the decision to stop investigations. He should implement an empathetic relation with the patient to announce the diagnosis and during all the follow-up. Some patients should be examined by a psychiatrist because up to two thirds have psychiatric comorbidity. Our series underline the importance for the neurologist to know these disorders in order to establish a comprehensive diagnostic approach and an appropriate medical care.

Disclosure: Nothing to disclose

EP1042

Cognitive impairment in transthyretin-related familial amyloid polyneuropathy

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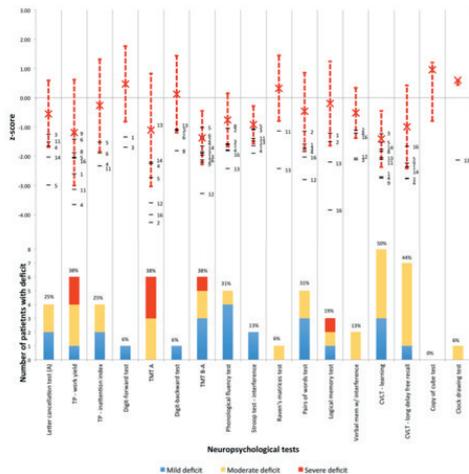
Background and aims: Transthyretin-related amyloidosis is typically characterized by a progressive neuropathy, cardiomyopathy, nephropathy and ocular disease. More than 90% of amyloidogenic transthyretin is produced by the liver, however this protein is also synthesized in the choroid plexus. Although some patients have transitory neurologic events the impact on cognition is still unknown. The goal of this work was to study the cognitive performance of TTR-FAP V30M patients.

Methods: A prospective observational study of a consecutive sample of patients with 10 or more years of disease duration was conducted. All patients undertook a extensive neuropsychological evaluation.

Results: Sixteen patients were included, with a mean age of 53-year-old and mean duration of disease of 18 years. All had been submitted to liver transplantation. The global status was not incapacitating in the majority, with 75% needing at most a stick to walk in and 38% were still actively working. The neuropsychological evaluation disclosed episodic memory impairments in 31% and executive dysfunction in 25% of patients.

DEMOGRAPHIC AND CLINICAL DATA					
	Mean	Standard deviation	Median	Quartile 1	Quartile 3
Age	53	12	Clinical Staging of TTR-FAP	II	I
Education (in years)	12	4	PND disease staging	IIIa	II
Disease duration (in years)	18	6			IIIa
Years of transplantation	14	4			
NEUROPSYCHOLOGICAL DATA BY DOMAIN					
	Attention	Executive functions	Memory	Visuoconstructive functions	
Patient 1		IMPAIRED	IMPAIRED		
Patient 2		IMPAIRED	IMPAIRED		
Patient 3		IMPAIRED	IMPAIRED		
Patient 4	IMPAIRED	IMPAIRED	IMPAIRED		
Patient 5	IMPAIRED				
Patient 11	IMPAIRED				
Patient 13		IMPAIRED			
Patient 16			IMPAIRED		
NEUROPSYCHOLOGICAL DATA BY TEST					
	Mean	Standard deviation	Number of patients with deficit		
			Mild	Moderate	Severe
Letter cancellation test (A)	-0.55	1.14	2	2	0
TP - work yield	-1.2	1.81	1	3	2
TP - inattention index	-0.26	1.58	2	2	0
Digit-forward test	0.47	1.29	1	0	0
TMT A	-1.1	1.93	0	3	3
Digit-backward test	0.12	1.31	1	0	0
TMT B-A	-1.37	0.92	3	2	1
Phonological Fluency test	-0.76	0.91	4	1	0
Stroop test - interference	-0.92	0.65	2	0	0
Raven's matrices test	0.32	1.12	0	1	0
Pairs of words test	-0.46	1.31	3	2	0
Logical memory test	-0.2	1.44	1	1	1
Verbal mem w/ interference	-0.52	0.86	0	2	0
CVLT - learning	-1.41	0.96	3	5	0
CVLT - long delay free recall	-1	1.42	1	6	0
Copy of cube test*	0.96	-0.8 - 1.2	0	0	0
Clock drawing test*	0.6	0.44 - 0.6	0	1	0

Demographic, clinical and neuropsychological data



Top – Mean (x) and standard deviation of z scores for each neuropsychological test. Each dash represents an individual with a z-score below -1; different numbers represent different patients. Bottom – Frequency of deficit in each test; different colors represent distinct levels of impairment.

Conclusion: These novel findings suggest that cognitive dysfunction can be a delayed manifestation of Familiar Amyloid Polyneuropathy. The putative relation of cognitive dysfunction with transthyretin-amyloid deposition can provide another model to study the amyloid hypothesis of cognitive impairment.

Disclosure: Nothing to disclose

EP1043
Cancelled

EP1044
Should the Mini Mental State Examination be considered as the best option for screening of cognitive impairment in lower educated individuals?

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Background and aims: Educational level is the most important determinant of performance on Mini Mental State Examination (MMSE) and cultural differences may account for different cutoffs points for each educational level. The Brief Cognitive Battery (BCB) has proven to be more appropriate in our midst. Thus, we aimed to compare the impact of the educational level on both the MMSE and the BCB.

Methods: 112 outclinic patients between 60 and 80 years of age were randomly chosen in a tertiary public hospital to enroll this study. We excluded all subjects who had a previous history of neurologic or psychiatric compromise. Subjects were divided in four groups according to education: illiterates, 1 to 4 years of education, 5 to 8 years and those with >8 years. All subjects were evaluated with both cognitive tests on the same day.

Results: Schooling had an influence on both MMSE scores ($p < 0.0001$) and individual performance on the clock drawing test ($p < 0.0001$). Educational level also had an impact on verbal fluency testing ($p < 0.00035$) of the BCB, but only for those subjects with higher scores obtained in the group with >8 years of education. Conversely, late recall test scores of the BCB were not influenced by educational level ($p = 0.0804$).

Conclusion: Educational level seems to interfere more on overall MMSE than on the BCB in all educational levels. Verbal fluency and the late recall tests of BCB showed impartial results. BCB seems to be a better assessment tool for our population and should be studied in other countries.

Disclosure: Nothing to disclose

EP1045

Cancelled

EP1046

see page 268

EP1047

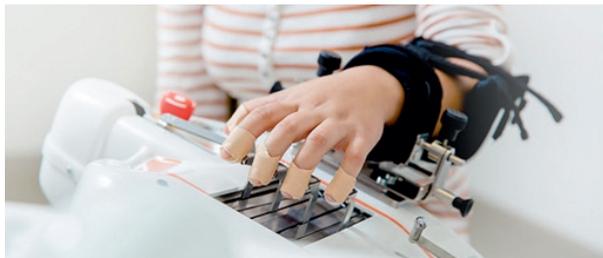
The effect of high-frequency repetitive transcranial magnetic stimulation of left dorsolateral prefrontal cortex on the motor learning

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Background and aims: Left dorsolateral prefrontal cortex (IDL PFC) plays crucial role in motor learning including working memory and attention. Repetitive transcranial magnetic stimulation (rTMS) may modulate cortical excitability with long-term effects, but effects of rTMS of IDL PFC in healthy volunteers are variable.

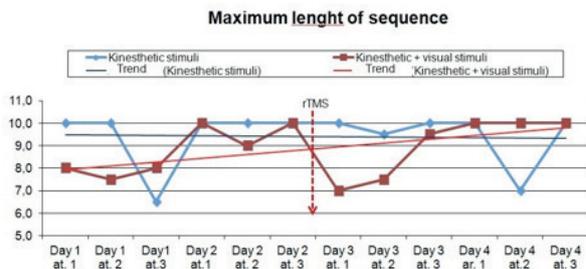
The study aimed to assess effects of high-frequency rTMS of IDL PFC on motor learning.

Methods: Ten healthy volunteers (mean age 27.5+/-5.8 years) completed 4-day course of working motor memory trains with mechanotherapeutic device (Fig. 1). In first series kinesthetic stimuli (finger support's movements) were presented one by one randomly, and volunteer had to memorize and repeat the sequence. In second series a combination of visual (finger image on screen) and kinesthetic stimuli was presented. Subjects performed three attempts in each series. Before the third train each subject received one session of navigated rTMS of IDL PFC (20Hz, 80% RMT, 2400 stimuli). Maximum length of sequence, which subject was able to perform, was assessed. We used Schulte test for attention evaluation on Day 1, after rTMS (Day 3), on Day 4.

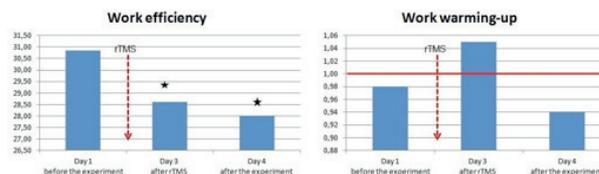


Mechanotherapeutic device that was used for motor memory trains. Right thumb and fingers tips were attached to the fingers support. Finger support's movements were presented as a kinesthetic stimuli.

Results: High-frequency rTMS of IDL PFC interrupts motor working memory processes in combination of visual and kinesthetic stimuli presentation but not in kinesthetic stimuli presentation alone (Fig. 2). rTMS improves attention efficiency but increases the work warming-up (Fig. 3



Maximum length of sequence results. rTMS is showed with a red arrow.



Schulte test results: work efficiency improvement and work warming-up deterioration is observed after the stimulation. rTMS is showed with a red arrow.

Conclusion: rTMS has different effects both on working memory (depending on modality of presented stimuli) and attention.

Disclosure: Study supported by Russian Foundation for Basic Research grant 15-04-08686A.

EP1048

Mental Imagery manipulation in multiple sclerosis

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Background and aims: A mental image is the representation in a person's mind of the physical world outside. Motor imagery (MI) can be defined as "a dynamic state during which a subject mentally simulates a given action" and was recently shown to be a promising tool in neurorehabilitation. However the ability to correctly perform MI may be impaired in patients with neurological dysfunction. Aim of our study is to assess mental images abilities in multiple sclerosis (MS) patients and healthy subjects with a particular attention to MI.

Methods: Patients with Relapsing-Remitting MS (RR-MS) and age, sex and education matched healthy controls underwent a Computer-based Mental Imagery Task (COMIT) to assess mental manipulation of visual (letters) and motor stimuli (hands, front and back view bodies). Results were compared using ANOVA, and Bonferroni multiple comparison's test. P values of less than 0.05 were considered statistically significant.

Results: We enrolled 20 RR-MS patients and 20 controls (Table 1). We found different results for group (F=4.91;p=0.033), orientation (F=52.09;p<0.001), task (F=9;p<0.001), and a significant interaction between task and orientation (F=2.68;p=0.005). Patients showed significant differences in reaction times for all tasks (hands and bodies) except for the letter task, suggesting a preserved object analysis in MS and an impaired MI.

	Patients	Healthy Subjects
Age (m, sd)	35 ± 9	33 ± 9
Sex (n, m, sd)		
M	10, 32 ± 9	10, 31 ± 8
F	10, 37.4 ± 9.1	10, 35.2 ± 9.9
Education (m, sd)	12.1 ± 3.8	12 ± 4
EDSS (m, sd)	3 ± 1	
Disease duration (m, sd)	10 ± 7.5	

Conclusion: We found a slower information processing speed in MS especially for hands and bodies manipulation. Further studies should investigate correlation between MS features, cognitive performance and MI, and how this influences response to rehabilitation.

Disclosure: Nothing to disclose

EP1049

Baseline characteristics and natural course of Thai patients with dementia

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Background and aims: More than half of patients with dementia lived in countries with low and middle incomes. However, there have been few studies on the natural course of disease in these countries. The purpose of this study was to study the baseline characteristics, natural course, and complications in Thai patients with dementia.

Methods: Patients with dementia who were treated in neurologic and psychiatric clinic from September, 2004 – February, 2016, were included. Data about natural course of diseases, behavioral and psychological symptoms in dementia (BPSD) and complications were studied.

Results: 207 patients were included. Mean age was 77-years-old. Mean Thai Mental State Examination (TMSE) was 17.5. Alzheimer's disease was the most common cause of dementia (55%). With the mean follow-up of 39 months (range from 2-126 months), 64% of the patients had BPSD. Sixty-two patients (30%) had complications required admission. Seven patients died. Fifty-four patients (29%) ended in the advanced stage of dementia. Mean duration from diagnosis to the advanced stage was 49 months. Complications that required admission usually occurred in moderate to severe dementia and were strongly associated with the advanced stage or death (OR 6.1, 95%CI 2.57-14.49, p-value <0.0001).

Conclusion: Alzheimer's disease was the most common cause of dementia in the study. BPSD was also commonly found in the patients. Most demented patients presented in moderate severity of dementia. Mean duration from diagnosis to the advanced stage of dementia was approximate 4-5 years.

Disclosure: Nothing to disclose

EP1050

Transient global amnesia: An altitude sickness?L. Erba¹, A. Czaplinski²¹*Cantonal Hospital Aarau, Aarau, Switzerland,*²*Neurozentrum Bellevue, Zurich, Switzerland*

Background and aims: Transient global amnesia (TGA) is an episode of acute onset of transient global anterograde memory deficit without other neurologic symptoms. Uncertainty still remains as to the etiology of TGA. The Regional Hospital in Davos reported an unusually high incidence of TGA. As the town of Davos is located at a relatively high altitude of 1560 m.a.s.l we hypothesized that altitude and low temperature may play a role in triggering the onset of TGA.

Methods: Retrospective study on the TGA events documented in the Regional Hospital Davos between 2005-2014. We analysed the following meteorological data: temperature, mean atmospheric pressure at sea level (P), mean relative humidity (RH), mean water vapour pressure (WVP) for all the days - regardless if there were documented TGA cases on those days or not.

Results: The TGA incidence in Davos (12/100'000/year) was higher as compared to the incidence quoted in the literature. We observed a peak of TGA occurrence in the winter. We found a significant relation between the mean day temperature and the incidence of TGA. The mean temperature in days with TGA cases was -1.1°C and in days without TGA cases 6.5°C (p-value <0.0001). There was no significant difference of occurrence of TGA in relation to the atmospheric pressure, wind and humidity.

Conclusion: We could illustrate that a peak of TGA cases occurs in winter and it seems the low temperature could be a trigger for TGA. Sympathetic activation due to cold may also play a role in the pathogenesis of TGA.

Disclosure: Nothing to disclose

EP1051

Experience of using meldonium in treatment of mild vascular cognitive impairment

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Background and aims: Neuropathological studies of mild cognitive impairment reveal a large load of vascular ischemic brain lesions. Therefore we have explored effect of antioxidant drug meldonium (Mildronat) in patients with vascular cognitive impairment.

Meldonium (Mildronat) is a licensed medical drug used widely throughout Eastern Europe and Central Asia for a number of cardiovascular conditions and is the basis of much debate in the world of sports doping.

Methods: 120 patients (72 female, 48 male, average age 71.6 years) with vascular cognitive impairment received meldonium 1000 mg i/v for ten days and then continued treatment orally for 6 months. Main clinical manifestations were impaired attention and forgetfulness, psychomotor slowing, impaired executive and visuospatial skills, change in personality, and emotional disturbance. The patient closely followed clinically, with repeated neuropsychological assessment. Results compared with a control group (N=135).

Results: The benefits of treatment began to be apparent within the first months. 46 patients showed stable improvement in cognitive performance measures and in daily life. 40 patients trend back to their baseline. 34 patients had no improvement after treatment. There was no case of worsening disease or bad drug bearing. Statistically significant reduction in cognitive impairment was seen in the treated group in the domains of memory, attention and executive functions.

Conclusion: It is concluded that meldonium may be recommended for the complex treatment of ischemic disorders of the cerebral circulation, include vascular cognitive impairment. The use appears to be effective and safe.

Disclosure: Nothing to disclose

EP1052

Feasibility of individual diagnostic approach for patients with chronic disorders of consciousness

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Background and aims: Chronic disorders of consciousness (DOC), such as VS and MCS, are diagnosed mostly by clinical examination, that carries high risk of misdiagnosis. New tools may help establish level of consciousness in certain cases, as presented here.

Methods: Case. A clinically VS patient A., male, 48 y.o., 2 years after intracerebral hemorrhage (CRS-R=10) showed only reflex movements to stimulation, no environment contact and preserved sleep-wake pattern. It was reported recently that presence of default mode network (DMN) signal on rs-fMRI was correlates with the degree of clinical consciousness impairment (Vanhaudenhuyse, 2010).

Results: On rs-fMRI (3T) we found activation of DMN areas (mPFC, PCC, LIPC, RIPC) (Fig.1). We also performed TMS-EEG with calculating Perturbational Complexity Index (PCI) - an independently validated promising consciousness metric (Casali, 2014), that allows reliable stratification of unresponsive patients with empirical cutoff level for discrimination between the unconscious and conscious states of 0.31 (Casarotto, 2016). We found out high complexity of the cortical response for the TMS stimuli, with PCI of 0.345 for frontal region stimulation (Fig.2) and 0.424 for parietal region (Fig.3) stimulation which implies the «conscious» state in this patient

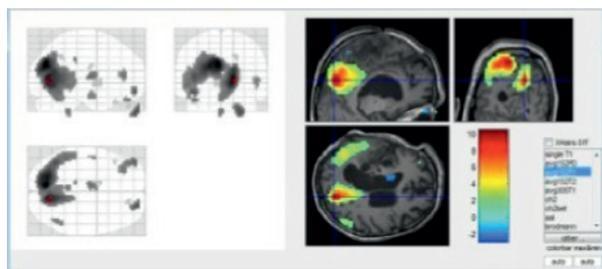


Fig.1. resting state fMRI data.

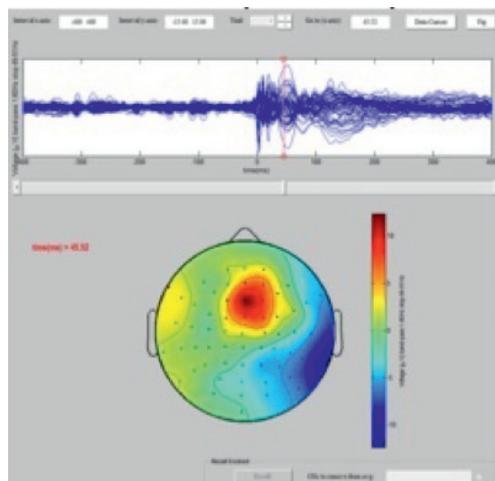


Fig.2. TMS-EEG Frontal stimulation response

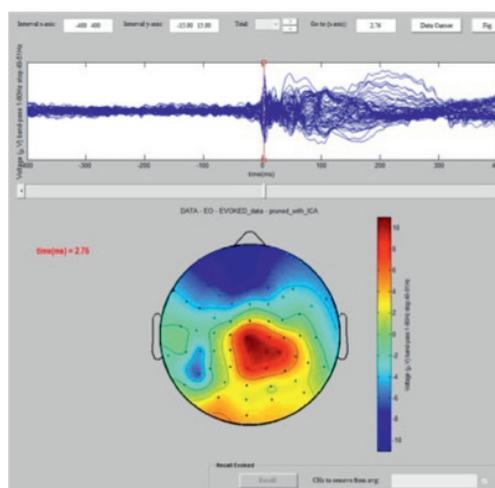


Fig.3. TMS-EEG Parietal stimulation response

Conclusion: novel diagnostic techniques may reveal patients with possible higher level of consciousness than seen clinically. Such patients should become subject for further investigation to find out the cause of discrepancy between clinical and neurophysiological results, as well as for intensive rehabilitation interventions.

Disclosure: The study is supported by Russian Scientific Foundation grant №16-15-00274.

EP1053

A challenging case of sporadic Creutzfeldt-Jakob disease: Confounding and evolving findings

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Background and aims: Rapidly progressive dementia poses a diagnostic challenge. We present a case of sporadic Creutzfeldt-Jakob Disease (sCJD) with atypical laboratory features.

Methods: A sixty-four-year-old male presented with a two month history of blurred vision and cognitive impairment progressing over six weeks. Initial examination revealed nystagmus and ataxia. In view of possible autoimmune encephalitis, corticosteroids, plasma exchange and cyclophosphamide were sequentially administered in the setting of new clinical features including myoclonus, pyramidal features, cogwheel rigidity and increasing frontal behaviour. However he deteriorated becoming mute, bedbound and died forty-nine days later.

Results: Vasculitic and infective screens were negative. Cerebrospinal fluid (CSF) examination revealed elevated protein (1.41g/L). 14-3-3 assay was weakly positive but real-time quaking induced conversion (RT-QuIC) assay was negative. Tau protein was markedly elevated. Glycine receptor (GlycR) antibodies were present in serum whilst other antibodies against neuronal surface antigens were negative. Serial MR Imaging demonstrated evolving cortical ribboning and diffusion restriction of the left caudate nucleus. Initial electroencephalogram was consistent with encephalopathy, later demonstrating frontal dominant periodic sharp-wave complexes.

On the basis of treatment-refractory deterioration, radiological and electrophysiological evidence, a diagnosis of probable sCJD was made. Interestingly, the RT-QuIC was positive on re-testing at a different dilution.

Conclusion: In the setting of rapidly progressive dementia, immunosuppression trial may be appropriate, although it is recognised neuronal antibodies can be positive in sCJD. This case is unusual for the presence of GlycR antibodies and markedly elevated CSF protein. This highlights the complex challenge of establishing the aetiology in such cases and interpreting the significance of laboratory findings.

Disclosure: Nothing to disclose

Education, History, Arts & Ethics

EP1054

SONAR identifies registrar research training needs in a clinical training program

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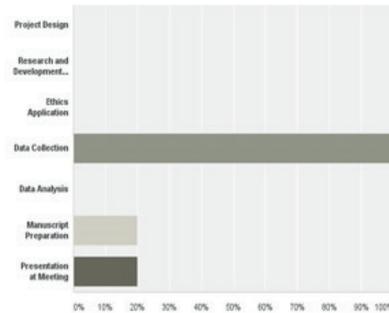
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Background and aims: Successful Trainee Clinical Research Networks have been established since 2007 and are primarily run by Surgical and Anaesthetic Trainees. In the southwest peninsula we have set up the first UK Neurology Trainee Audit and Research Collaborative to deliver clinical studies. Ensuring all trainees have appropriate training is a key requirement; we aimed to ascertain the training need of our network members.

Methods: A survey was sent to all 9 neurology trainees in the Peninsula Deanery. It comprised 5 questions to establish trainee clinical research training and experience.

Results: Response rate was 100%. Training level varied from ST3-5; 22% had previously completed higher degrees. 40% of trainees had not been involved in clinical research. One trainee had not had formal good clinical practice (GCP) training and none had formal Informed Consent training. Of those who had been involved in research, there had been limited involvement in project design, ethics approval processes, data analysis, manuscript preparation or findings presentation.

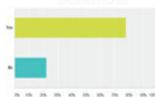
Q5: If you have been involved in research, please tick which aspect?



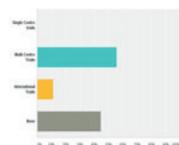
Conclusion: We identified a training need in our Trainee Audit & Research Network. In order to address this, we have organised formal GCP & Informed Consent training; to broaden the research experience of network members, we are planning our first collaborative research project.

Disclosure: Nothing to disclose

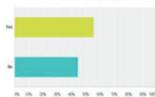
Q3: Do you feel you have had good opportunities to be involved in clinical research?



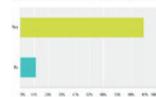
Q4: Have you been involved in..



Q1: During your Neurology Training so far have you been involved in clinical research?



Q2: Have you had any formal training in clinical research methodology (GCP/informed consent)?



EP1055

Integration of international physicians in Germany: An empirical study in the acute-neurological departments in Westphalia-Lippe

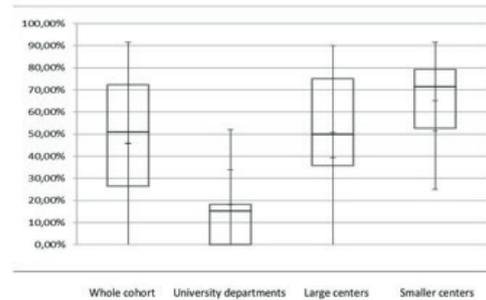
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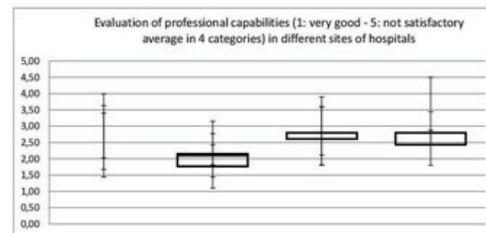
Background and aims: Demographic changes and technical innovations increase the demand for physicians in industrialized countries. Since 1990 medical schools in Germany barely increased capacities, so increasing numbers of physicians are immigrating to fill this gap. The Chamber of Physicians of Westphalia-Lippe, where 8.3 million inhabitants cared by more than 32,000 physicians, hosts a proportion of 15.6% of international physicians. 44% of physicians in specialty training immigrated from non-German speaking countries. Hospitals outside larger cities face increasing difficulties to recruit their physician staff.

Methods: All neurological departments accredited for complete neurological specialty training were included, 30/38 participated in a survey and detailed interview. Data of health economic performance and staff recruitment were collected including anonymized data about all international residents, including professional performance and dismissals.

Results: 27 of 30 neurological departments employed international physicians (range 7 – 92% of all residents). The difference between University-Departments and larger and smaller centers was significant ($p=0.009$) (figure 1). The same was shown concerning the evaluation of knowledge, skills, language abilities and social competences (figure 2). 220 international residents were individually rated and 56 dismissals analysed: Physicians from Balkan countries had the highest risk (47%) followed by arab-oriental countries (39%).



Graph 1: Percentage of international residents among Neurological departments



Graph 2: Whole cohort University departments Large centers Smaller centers

Conclusion: The shortage of German medical graduates leads to marked immigration of international physicians. Neurological departments outside metropolitan areas have immense problems to recruit qualified residents in training concerning to their professional abilities. This leads to high dismissal rates and compromises the quality of care in German neurological departments outside big cities.

Disclosure: Nothing to disclose

EP1056

The Dynamic Dutch Guideline for Epilepsy

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Objective: To develop a Dutch Dynamic Guideline for Epilepsy.

Methods: A clinical practice guideline (CPG) has to be accessible and practical. We developed a modular web-based CPG in which 23 diagnostic and therapeutic modules are listed, with answers to 57 key questions, resulting in 189 recommendations. Questions and recommendations in each module are presented briefly under a first tab. For further reading, other tabs include "summary and grading of the literature"; "references"; "considerations"; "expert opinion" and "information on economics". A reference list with hyperlinks to abstracts is included. Updates, such as studies published after authorization of the latest CPG version, are presented under the tab "new literature", which will then be processed in a subsequent edition. Grading of evidence is made transparent by adding evidence-scoring tables (using GRADE for therapeutic and EBRO for diagnostic studies). Development of this CPG was accompanied by an implementation procedure which included the following actions:

- guideline users are encouraged to submit requests for the development of new modules;
- indicators of good care are formulated and put on the website;
- questions for the obligatory annual exam for Dutch neurologists are retrieved from the guideline;
- annual national courses on epilepsy for residents in neurology and pediatrics are based on knowledge of the CPG.

Results: An exclusively web-based and annually updated Dutch CPG (first edition in 2013). Currently, <http://epilepsie.neurologie.nl> is accessed 2000 to 3000 times each month.

Conclusion: The development and maintenance of a dynamic guideline with yearly updates is feasible.

Disclosure: Nothing to disclose

EP1057

Incorporating economic evaluations in clinical practice guidelines: A standard approach to increase quality and to reduce workload for guideline developers

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Background and aims: Clinical practice guidelines (CPG's) serve as a roadmap for evidence-based treatment of patients with specific diseases. Although recommended, currently economic evaluations (EE's) are not routinely incorporated in these CPG's. We developed a standard approach to incorporate EE's into CPG's.

Methods: This approach provides an overview of all knowledge and practical information needed to systematically incorporate EE's in CPG's. Specifically, a flowchart containing five steps of the review process: guidance on the development and selection of search strategies, guidance on selection of different databases, information on how to select and use checklists to appraise the methodological quality of the studies, information on how to handle transferability and generalizability issues, guidance on data extraction and data syntheses. In addition, ready to use standard tables for data extraction, a list of existing databases and advice about how to manage references is given.

Results: The five step approach is used to incorporate EE in the Dutch CPG for Epilepsy. This approach facilitates annual actualization of the CPG. Moreover it increases transparency and standardization of performing systematic reviews of with a maximum efficiency for guideline developers.

Conclusion: The use of a standardized approach facilitates the incorporation of EE's in new and existing CPG's. The standardized approach is feasible, ensures reproducibility and minimizes the workload needed. The five step approach is successfully implemented in the Dutch CPG.

Disclosure: Nothing to disclose

EP1058

Health promotion in the field of neurology according to European junior neurologists – an EAN-Resident and Research Fellow (RRFS) survey

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Background and aims: Health promotions (HP) such as exercise, reduced alcohol consumption, smoking cessation, diet may play a role in primary and secondary prevention of different neurological disorders, especially in common conditions such as dementia and stroke, which have an essential global public health and social care burden. Our study focuses on the opinion of European residents and junior neurologists (RJN) on HP.

Methods: An anonymous online survey was distributed among RJN between 1 May 2016 and 31 December 2016. The survey also included a short description about HP.

Results: 98 RJN (66.7% female) from 25 countries completed the survey. The majority (67%) had heard about HP before, but 33% had not. Almost all (99%) agreed on the importance of HP in the management of neurological disorders. However, only a minority of the residency programs offered training on HP (24.5%). The RJN strongly agreed that reduced alcohol consumption (77.6%), smoking cessation (76.5%), diet (52%), exercise (64.3%), stress management (60.2%) and depression treatment (45.9%) can decrease the burden of neurological disorders. Table 1 summarizes which barriers make HP challenging. Despite these difficulties, (99.1%) of RJN would encourage their patients to participate in HP offers.

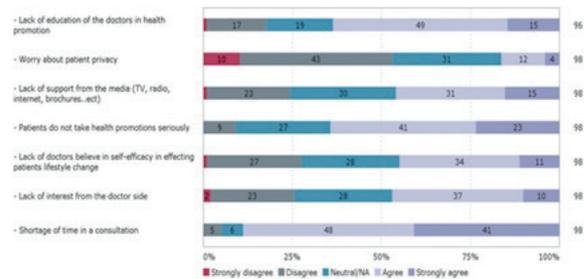


Table 1: Distribution of the answers on "What kind of barriers make health promotion challenging?".

Conclusion: The survey clearly outlines that RJN agree on the importance of HP for the management of neurological disorders. Appropriate training during residency, sharing up-to-date knowledge about HP effect on the neurological diseases, is recommended.

Disclosure: Nothing to disclose

EP1059

Mursili II: First historical primary progressive aphasia case?

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Background and aims: Historical neurology studies usually aim to reach diagnosis by old case information and available additional data. The Hittites were an Ancient people establishing an empire in north-central Anatolia around 1600 BC. Among their kings, Mursili II left the highest number of documents, and a number aspects of his rein (plague, other epidemics and septicemia, religious personality, "wives of Mursili" etc.) have been studied

Methods: As explained below; Mursili had to live with a language/speech impairment at a certain part of his life. On the documents written he explains this occurred after a fear he experienced due to a thunderous storm during his walk. A difficulty/ impairment of speaking occurs, which in time progresses to almost a loss of speech ability. To find the cause of his illness he applied to fortune telling. According to history books, this speech impairment started as dysarthria and gradually progressed.

Results: Basically we do not know the progression time of the illness but probably it is probably not too long. With the present information, nonfluent (Agrammatic) form of Primary Progressive Aphasia (PPA) seems to be the most likely diagnosis. Adults of any age can develop PPA, but it is more common under 65. Patients have a different language symptoms and cases are not same. The initial symptoms include slowed/ halting speech, decreased use of language, word-finding hesitations, using words that are incomprehensible, all of which may have been Mursili's original symptoms

Conclusion: Possibly this one of the greatest kings of Hittites was also the first written (cuneiform) described PPA case.

Disclosure: Nothing to disclose

EP1060

Cauterization in the treatment of neurological diseases by famous physicians like Brown-Séguard and Charcot

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Background and aims: Cauterization is one of the oldest means of treatment. The most frequent indication is pain in general. Cauterization is still practiced in folk / primitive medicine in the world.

Methods: During my 12 years of employment in the Kingdom of Saudi Arabia and travelling to many Arab countries, I came in touch with cauterized patients and their healers. Since 1989, I built up an extensive collection of world literature related to cauterization. The Greek and Arab medicine describing the use of cautery for neurological diseases. The 19th and 20th century literature is reporting of cauterization for neurological diseases like paresis, epilepsy by famous neurologists like Charcot and Brown-Sequard. Also the general surgeon Bier was in favour of cautery.

Results: I will present the literature describing the indication for cauterization in neurological diseases by Brown-Sequard and Charcot.

Conclusion: The names of these physicians are world famous and daily used for syndromes. However, most of us do not know that they practised cautery for neurological diseases. I believe it is worth full to report this to the neurological – neurosurgical community

Disclosure: Nothing to disclose

EP1061

Hypercreativity and changes in artistic style as debut of frontotemporal dementia

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Background and aims: The change in artistic style and hypercreativity has been described in frontotemporal dementia (FTD). We present a case of compulsive creation of pieces of arts as the first manifestation of FTD.

Methods: A 65-year-old man, administrative and an amateur artist, was admitted to our hospital with diplopia, ptosis and general weakness. He was diagnosed with Myasthenia Gravis, and was discharge. During the admission, the patient showed an amazing compulsive behavior: he created 63 songs with a scatological and erotic theme. Additionally, he changed his pictorial style: he used to paint classical scenes (figure 1) but by this time, he only wanted to paint erotic pictures (figure 2). He had not any other symptoms. A neuropsychological test showed an executive dysfunction and a brain MR showed frontal lobes atrophy.

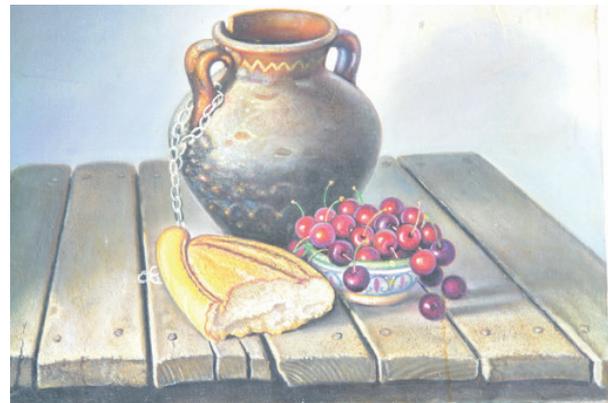


Figure 1

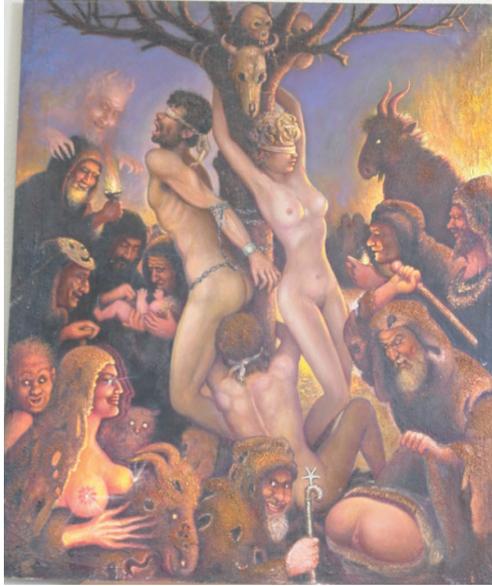


Figure 2

Results: Five years later, his family advised that he had an abnormal behavior: disinhibition, impulsive actions and euphoria. His compulsive manner of write songs was worsening: he wrote more than 3000 songs of erotic theme, and performed a big sculpture with a lot of scabrous details that he called “pictorial-sculpture” (figure 3).

Finally, the patient was diagnosed with probable behavioral variant FTD, accordingly with the current diagnosis criteria.



Figure 3

Conclusion: The most patients with FTD show a diminution in creativity. However, some patients show a hypercreativity in arts; change their artistic style or even start a new creative ability. This lack of limits or transmodal creativity has been described in FTD.

Disclosure: Nothing to disclose

EP1062

“The metaspurochaetosis is the meningeal process”: Neurosyphilis as the driving force of Thomas Mann’s Doctor Faustus

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Background and aims: Thomas Mann’s Doctor Faustus is one of the undisputed pinnacles of German literature for its insight on the creative process of an artist; at its core, however, lies the influence of neurosyphilis, one of syphilis’ most devastating forms. Several classical composers, such as Smetana, Schumann and Donizetti, were victimized by it; in his novel, Mann offers the case of fictional composer Adrian Leverkühn.

Methods: Mann’s book, European and American guidelines on syphilis were reviewed.

Results: Disease plays a major role in Thomas Mann’s oeuvre, from The Magic Mountain to Death in Venice. In Doctor Faustus, however, the correlation is at its closest. The aspiring composer Adrian Leverkühn comes into contact with a prostitute early in the book and develops a “local infection” afterwards. In chapter XXV, Leverkühn describes his encounter with a Mephistopheles-like entity, perhaps an hallucination from secondary meningo-encephalitis, who reveals his infection by “our livid Venus, the Spirochaeta pallida”, giving him 24 years of unmitigated musical genius inspired by the auditive and visual hallucinations of neurosyphilis. After the disease’s latent period, he develops Argyll-Robertson pupils, “which always had the same size, (...) were never changed by differences in light”, and a prolonged demential period of ten years before his death, parietic and insomniac.

Conclusion: Mann’s Leverkühn is a fictional character whose musical brilliance can be attributed to hallucinatory effects of neurosyphilis. Mann’s text provides the careful reader clues to the true nature of his ailment, from descriptions of abnormal neurological findings (Argyll-Robertson pupils) to a more florid description of neuropsychological symptoms.

Disclosure: Nothing to disclose

EP1063

The neurological disease as a muse of famous writers

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Background and aims: Some important writers suffered from neurological diseases. We investigated whether their neurological condition could have influenced their artistic production.

Methods: Search for relevant links between neurological diseases and literary output of famous writers.

Results: Friedrich Nietzsche suffered from neurosyphilis that led him into a deep sadness and introspection, what can be easily realized in his works. When Nietzsche became parietic, according to Freud, it "gave him the capacity[...] of seeing through all layers and recognizing the instincts at the very base". Guy de Maupassant also had neurosyphilis and there is consent that his creativity was changed as the disease progressed. Robert Sherard, in face of Maupassant's literary leap to fame in 1880, became certain that syphilis could take one to new heights. Lewis Carroll had migraine and experienced visual auras. Some studios rigorously affirm that his visual disturbances were the main influence to create the novel Alice's Adventures in Wonderland, that contemplate descriptions of metamorphopsias, distortions and bizarre characters. Gustave Flaubert was diagnosed with epilepsy, when he decided to isolate himself and dedicate more time to literature. Writing became an "outlet", as he once confessed, to his neurological condition that was cause of so much suffering. Charles Baudelaire had a left-hemisphere stroke and once wrote: 'I claim that inspiration is somehow linked to stroke...'. His aphasia would consecrate the expletive Cré nom and made him reinvent his artistic style. **Conclusion:** Neurological disease participated of the creativity process of important famous writers, playing a pivotal role in the genesis of eternal literary masterpieces.

Disclosure: Nothing to disclose

Epilepsy 1

EP1064

Patterns of use of Antiepileptic Drugs (AEDs) in a tertiary neurology clinic in Khartoum City, Sudan

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Background and aims: Patterns of use of antiepileptic drugs (AEDs) differ between developed and developing countries. In the latter, use of second generation AEDs is not common. To study the patterns of AEDs uses in terms of frequencies of use, treatment outcomes, and tolerability.

Methods: This is a retrospective cross-sectional study. A total of 360 adult Sudanese epilepsy patients who attended a tertiary neurology clinic in Khartoum city, Sudan between 2006 and 2010 were included.

Results: 76.1% of patients (274/360) were classified as drug responsive while 23.9% (86/360) were classified to have DRE. Out of 624 prescriptions, the five most frequently prescribed AEDs were carbamazepine (32.7%), sodium valproate (28.5%), phenytoin & lamotrigine (12.5% each) and phenobarbitone (6.2%). 44.1% (275/624) of prescriptions resulted in sustained seizure freedom for their first use whether as monotherapy or in combination, while treatment failure per individual drug was the reported outcome in 41.1% (256/624). In 12.5% (78/624) of the prescriptions, AEDs resulted in seizure freedom in their initial use. The highest rate of achieving seizure freedom during the first use was reported with phenytoin 63.3% (50/79), valproate 48.3% (86/178), carbamazepine 47.6% (97/204) and lamotrigine 21.8% (17/78). Reported treatment failure rates were: lamotrigine 66.7% (52/78), phenobarbitone 64.1% (25/39), valproate 37.6% (67/178), carbamazepine 28.8% (59/204) and phenytoin 24.1% (19/79). Adverse events were reported with 7.4% of prescriptions while AEDs discontinuation was necessary after 2.7% of prescriptions.

Patterns of Uses of Antiepileptic Drugs (AEDs) in A Tertiary Neurology Clinic in Khartoum City, Sudan

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Table 1 Patterns of treatment outcome for individual AEDs^a

Treatment outcome AEDs	Responsive	Failed	Responsive initially & turned to fail later	Responsive initially and for second time following re-administration ^b	Failed initially & then became responsive	Total Number of prescriptions
Carbamazepine	97 (47.6%)	59 (28.9%)	6 (2.9%)	21 (10.6%)	0 (0%)	204 (33.7%)
Valproate	86 (48.3%)	67 (37.6%)	4 (2.3%)	19 (11.2%)	1 (0.6%)	178 (28.5%)
Phenytoin	50 (63.3%)	19 (24.1%)	2 (2.5%)	4 (5.1%)	0 (0%)	79 (12.7%)
Lamotrigine	17 (21.8%)	52 (66.7%)	0 (0%)	4 (5.1%)	1 (1.3%)	78 (12.5%)
Phenobarbitone	13 (33.3%)	25 (64.1%)	1 (2.6%)	0 (0%)	0 (0%)	39 (6.2%)
Clonazepam	7 (28%)	18 (72%)	0 (0%)	0 (0%)	0 (0%)	25 (4%)
Topiramate	4 (25%)	12 (75%)	0 (0%)	0 (0%)	0 (0%)	16 (2.6%)
Levetiracetam	1 (50%)	1 (50%)	0 (0%)	0 (0%)	0 (0%)	2 (0.3%)
Acetazolamide	0 (0%)	2 (100%)	0 (0%)	0 (0%)	0 (0%)	2 (0.3%)
Gabapentin	0 (0%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)
Total	275 (44.1%)	256 (41%)	13 (2.1%)	78 (12.5%)	2 (0.3%)	624

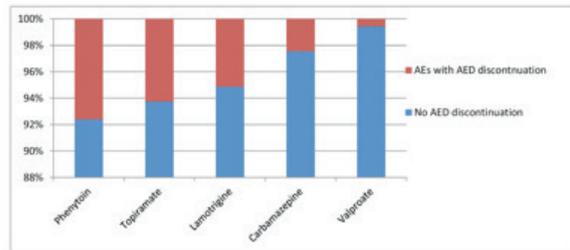
^a AEDs were considered in this table were only those which were appropriately used, with adequate trial durations and clinically effective dosage and without withdrawal secondary to adverse drug events.
^b As the number of AED prescriptions were considered in this table, the numbers in this column particularly were multiplied by 2 since every prescription to which there was a response has been prescribed in a different occasion and hence considered as a separate prescription

Patterns of Uses of Antiepileptic Drugs (AEDs) in A Tertiary Neurology Clinic in Khartoum City, Sudan

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Figure 1 Percentages of adverse events that led to discontinuation of AEDs when related to the total number of use of individual AEDs



Conclusion: First-generation AEDs are still dominating clinical practice in developing countries with comparable outcomes with second-generation agents.

Disclosure: Nothing to disclose

EP1065

Patterns of drug resistant epilepsy in a cohort of adult epilepsy patients

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Background and aims: Studying patterns of drug-resistant epilepsy enhances understanding its possible pathogenic mechanisms. To study the patterns of drug-resistant epilepsy (DRE) in a cohort of adult epilepsy patients.

Methods: This is a retrospective cross-sectional study. A total of 360 adult Sudanese epilepsy patients who attended a tertiary neurology clinic in Khartoum city, Sudan between 2006-2010 were included.

Results: 23.9% (86/360) of patients were classified to have DRE. Out of these 86 patients, 81.4% were found to have a constant resistant pattern while 18.6% were having an alternating pattern. No significant difference in clinical characteristics was found between the two patterns. When considering covariates related to AED therapy, constant pattern patients were found to have a significantly higher previous history of AED therapy (P=0.046). When tested for the duration of seizure freedom achieved, 35.7% of patients with the constant pattern have never become seizure-free in comparison with 18.8% of patients with the alternating pattern (P=0.191). Similarly, 50% of patients with the constant resistant pattern failed to respond to 3 AEDs in comparison with 34.3% of patients with the alternating pattern (P=0.684). Five detailed patterns of DRE were recognized: constant absolute resistant pattern (76.7%), constant partial resistant pattern (4.7%), primary responsive pattern followed by secondary absolute resistance (9.3%), primary responsive pattern followed by secondary partial resistance (2.3%) and primary absolute resistant pattern followed by secondary responsiveness (7%).

Patterns of Drug Resistant Epilepsy in A Cohort of Adult Epilepsy Patients

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Table 1 Characteristics of constant resistant pattern vs alternating patterns using cross-tabulation & Chi-square test

Covariate	Components	Constant resistant pattern (76 cases)	Alternating patterns (16 cases)	P value
Gender	Males	48 (66.6%)	11 (68.8%)	0.989
	Females	28 (33.4%)	5 (31.2%)	
Age at time of labelling as drug resistant or drug responsive	16 - 20 years	40 (50%)	11 (68.8%)	0.390
	20 - 25 years	15 (17.4%)	0 (0%)	
	26 - 30 years	7 (8.7%)	1 (6.2%)	
	31 - 35 years	2 (2.5%)	1 (6.2%)	
	36 - 40 years	1 (1.2%)	0 (0%)	
	41 - 45 years	1 (1.2%)	0 (0%)	
Residence	Central states	20 (26.3%)	1 (6.2%)	0.061
	Northern states	9 (11.7%)	2 (12.5%)	
	Eastern states	4 (5.1%)	0 (0%)	
	Western states	5 (6.3%)	0 (0%)	
Employment	Unemployed	20 (26.3%)	4 (25%)	0.668
	Student	22 (27.9%)	6 (37.5%)	
	Self-employment	17 (21.3%)	2 (12.5%)	
	Formal employment	4 (5.1%)	2 (12.5%)	
	Housewife	1 (1.2%)	2 (12.5%)	
	Retired	2 (2.5%)	0 (0%)	
	< 1 year	1 (1.2%)	1 (6.2%)	
	1 - 12 years	35 (44.9%)	7 (43.8%)	
Age at time of seizure onset	11 - 15 years	17 (21.3%)	3 (18.8%)	0.702
	16 - 20 years	16 (20.3%)	5 (31.2%)	
	21 - 25 years	1 (1.2%)	0 (0%)	
	26 - 30 years	1 (1.2%)	0 (0%)	
EEG findings	Normal	3 (3.7%)	3 (18.8%)	0.287
	Abnormal	15 (19.2%)	6 (37.5%)	
	Not indicated for diagnosis	1 (1.2%)	0 (0%)	
Brain imaging	Normal	37 (47.4%)	6 (37.5%)	0.433
	Abnormal	1 (1.2%)	0 (0%)	
	Not indicated for diagnosis	1 (1.2%)	0 (0%)	
Seizure type	Focal onset seizures	51 (65.9%)	11 (68.8%)	0.741
	Generalized seizures	19 (23.7%)	5 (31.2%)	
Aetiology	Genetic	19 (24.5%)	5 (31.2%)	0.753
	Structural/metabolic	20 (26.3%)	5 (31.2%)	
	Infective	22 (27.9%)	6 (37.5%)	
	Idiopathic	3 (3.7%)	0 (0%)	
Duration of epilepsy	1 - 10 years	36 (46.1%)	7 (43.8%)	0.993
	11 - 20 years	24 (30.4%)	6 (37.5%)	
	21 - 30 years	2 (2.5%)	2 (12.5%)	
Learning disability	Yes	20 (26.3%)	5 (31.2%)	0.831
	No	50 (63.7%)	11 (68.8%)	
Psychiatric illness	Yes	7 (9.1%)	2 (12.5%)	0.325
	No	69 (89.9%)	14 (87.5%)	

Patterns of Drug Resistant Epilepsy in A Cohort of Adult Epilepsy Patients

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Table 2 Comparison between constant resistant pattern and alternating pattern in relation to treatment related factors

Covariate	Components	Constant pattern of resistance (76 cases)	Alternating patterns (16 cases)	P value*
Previous AED therapy	Yes	56 (80%)	9 (56.3%)	0.046
	No	14 (20%)	7 (43.7%)	
Seizure freedom has never been achieved even for a single month	Yes	25 (35.7%)	3 (18.8%)	0.191
	No	45 (64.3%)	13 (81.2%)	
Number of AEDs failed	2 AEDs	24 (34.3%)	8 (50%)	0.684
	3 AEDs	35 (50%)	6 (37.5%)	
	4 AEDs	7 (10%)	1 (6.25%)	
	5 AEDs	4 (5.7%)	1 (6.25%)	
	Adverse events as a result of AED therapy	Yes	18 (25.7%)	
No	52 (74.3%)	14 (87.5%)		

*Significant P values in bold

Conclusion: These findings indicate that AED pharmacoresistance is a heterogeneous status.

Disclosure: Nothing to disclose

EP1066

Electrical status epilepticus during sleep – a study of 71 Bulgarian patients

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Background and aims: The aim of the study was to analyse the clinical course and the treatment approaches in patients with electrical status epilepticus during sleep (ESES).

Methods: We have retrospectively reviewed the medical data of 51 children with idiopathic ESES and 20 children with symptomatic ESES, treated between 2006 and 2015 in the Clinic of Child Neurology in Sofia, Bulgaria.

Results: The patients with idiopathic ESES showed a later epilepsy onset and more benign disease course than symptomatic cases. A permanent ESES remission was achieved with the initial treatment in 33.3% (15/45) of the children with idiopathic epilepsy, 19 cases showed relapsing and 11 cases – persistent course of ESES, 6 cases were not followed up in the clinic. Good results were achieved with: 1) corticosteroids (CS) (n=21) – permanent ESES remission in 3 and transient – in 14 children, 2) levetiracetam (LEV) (n=20) – permanent ESES remission in 7 and transient – in 3 children, 3) clonazepam (CZP) (n=15) – permanent ESES remission in 5 and transient – in 4 children, 4) ethosuximide (ESM) and sulthiame (STM). The patients with symptomatic epilepsy had more unfavourable evolution as 19 patients had persistent or relapsing course of ESES with only transient improvement with LEV (n=15, transient ESES remission in 9 children), CZP (n=8, transient remission in 3), CS (n=12, transient remission in 9) and ESM (n=5, transient remission in 3).

Conclusion: ESES is characterized by a significant therapeutic resistance, especially in the group of symptomatic epilepsies. The most effective anticonvulsants are CS, LEV, ESM and benzodiazepines.

Disclosure: Nothing to disclose

EP1067

Idiopathic focal epilepsies with occipital paroxysms

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Background and aims: The aim of the study was to analyze and compare the clinical course, EEG and treatment approaches in children with Gastaut (GS) and Panayiotopoulos syndrome (PS)

Methods: We have included 40 patients with PS and 13 – with GS, treated in the Clinic of child neurology in Sofia, Bulgaria.

Results: The children with PS had an earlier age of seizure onset (4y compared to 8y 9m in the cases of GS). Rare seizures (between 2 and 6) predominated in PS (in 65%) while half of the patients with GS had multiple seizures. The seizures were mainly nocturnal in PS (in 80%), while all the children with GS had diurnal seizures and only half of them experienced nocturnal seizures. The most common ictal presentation in PS was nausea and vomiting (in 95% of the cases) while visual symptoms were the main ictal manifestation in GS (visual hallucinations - in 84.6% of the children and visual loss – in 53.8%). The occipital epileptiform activity was the typical EEG feature in GS, but was described in only 57.5% of the patients with PS at the time of the diagnosis.

Conclusion: PS is characterized by a typical clinical presentation with rare, mainly nocturnal seizures with leading autonomic symptoms that show good response to treatment. Unlike PS the typical seizures in GS are brief, mainly diurnal and often multiple. Valproate and Carbamazepine are the drugs of first choice in GS and the treatment is usually long lasting due to the high risk of relapses.

Disclosure: Nothing to disclose

EP1068

Adult phenotype of Dravet syndrome associated with STXBP1 (syntaxin binding protein 1) mutation and good response to cannabidiol treatment

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Background and aims: We present a case of Dravet syndrome: adult phenotype with a STXBP1 mutation and its good response to cannabidiol treatment.

Methods: A 19-year-old woman with history of epilepsy since infancy and poor response to various anticonvulsant therapies. She presented a good psychomotor development until the two years of life, although to the six months had a first crisis which coincided with fever and was followed by motor deficit. Two years later she performed episodes of loss of head tone. From the age of 6, she has generalized seizures more than 10 times a day and from the age of 13 she associates reflexive crises after sound and tactile stimuli. Various genetic-metabolic tests were negative, including the mutation for the SCN1A gene (sodium voltage-gated channel alpha subunit 1). In the last year she has presented marked bradykinesia which impedes walking (FAC 1 according to the gait rating scale - Functional Ambulatory Classifier), mood swings, impulsivity associated with heteroaggressive behavior and visual hallucinosis.

Results: We required whole exome sequencing, finding mutation in the STXBP1 gene. We also suggested to initiate treatment with cannabidiol, achieving a considerable reduction in the number of crises in the day and an improvement in the ability to walk (FAC 4).

Conclusion: The mutation of STXBP1 gene proved to cause Dravet's syndrome in patients with negativity for the mutation of SCN1A. Our case is special because it presents the recent description of the adult phenotype of Dravet's syndrome moreover it is associated to good response to cannabidiol treatment.

Disclosure: Nothing to disclose

EP1069

Determination of social phobia, agoraphobia and depression frequency using clinical scales in epilepsy patients

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Background and aims: Patients with epilepsy can develop psychiatric disorders that decrease quality of life and increase suicide rate. Our study was designed to investigate depression, anxiety, social phobia, agoraphobia of epilepsy patients.

Methods: The study was done between September 2015 - September 2016 in Marmara University Pendik Research Hospital, Turkey, Neurology outpatient clinic, among 150 random patients (18-66 years old) and 70 controls with similar age and gender. Beck Depression Inventory (BDI), Liebowitz Social Phobia Inventory (LSPI) and Panic Agoraphobia Inventory were applied to both groups.

Results: Among evaluated results, 62,7% of the patients were women and their average age was 34.2 ± 10.9 , respectively 33.00 ± 10.2 for controls. Fifty percent of the education level of both patients and control group was primary and middle school. The score of BDI for the patients were 15.18 ± 12.25 , respectively 10.87 ± 9.06 for controls, that was statistically significant ($p=0.0038$). Both patient and control group were compared according to LSPI and subgroup analysis (for anxiety and avoidance), but no statistical significant result was found ($p>0.05$). Agoraphobia was more common among women and frequently panic attack occurred in closed areas as elevators, tunnels, airplane or subway.

Conclusion: Our results showed that depression and agoraphobia were more common with epileptic patients compared to control group and often seen among women. In epileptic patients, psychiatric deficiencies are frequently ignored and not treated properly. It is very important to identify and treat comorbid factors in order to increase patient's quality of life.

Disclosure: Nothing to disclose

EP1070

Ambulatory EEG: A possible alternative to inpatient video-EEG?

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Background and aims: Ambulatory EEG (AEEG) has been suggested as an alternative to inpatient video-EEG which is particularly useful in assisting the differential diagnosis between epileptic and psychogenic nonepileptic seizures. The aim of this study was to examine the utility of ambulatory EEG (AEEG) in our outpatient clinic.

Methods: We did a retrospective analyses of clinical files and EEG recordings of consecutive patients referred to our neurophysiology department for AEEG studies from January 2011 to December 2015. AEEG recording was performed using a 19-channel recording system and electrodes were applied according to the International 10–20 electrode system. Patients were provided with a clinical diary. Recordings lasting 24 hours. We reviewed clinical files for purpose for the exam and any diagnostic or therapeutic alteration made after the exam.

Results: 58 patient, 30 (52%) male, median age 43 years (7-84 min-max) were included. The primary reasons for the AEEGs were subdivided into three categories: to differentiate between seizures and non-epileptic events (29 patients); to characterize seizure type or localization (20 patients) and to determine the frequency of seizures (9 patients). 84% of the exams had alterations, interictal epileptiform discharges (IEDs) in 67% and epileptic seizures in 4%. The diagnosis was changed in 12 (21%) patients (non-epilepsy for epilepsy in 9 patients) and 33 patients changed therapeutics.

Conclusion: In our series AEEG was a very useful tool, particularly in the differential diagnosis between seizures and non epileptic events. As in other studies our data highlights the role of AEEG as an alternative to a more expensive and less available video-EEG.

Disclosure: Nothing to disclose

EP1071

Comparison of corpus callosotomy and vagal nerve stimulation in treatment of pharmacoresistant epileptic encephalopathies

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Background and aims: Corpus callosotomy (CC) and vagal nerve stimulation (VNS) are palliative neurosurgical methods used in treatment of pharmacoresistant epilepsy in patients with unknown, multiple or epileptogenic zones in eloquent brain areas where no resectable surgery is possible.

Methods: We conducted a retrospective research in patients with generalized epilepsy (GE) non responsive to medical treatment in whom either CC or VNS was done. All patients were followed up through one year. The total number of patients was 20, divided in two groups, CC (n=8, mean age 20) and VNS (n=12, mean age 31) group. In the first group all patients, except one who had postencephalitic seizures, had Lennox-Gastaut syndrome (LGS), while in the second one 25% had LGS, 25% had progressive myoclonic epilepsy and 50% had other epileptic encephalopathies.

Results: We observed the effect of CC or VNS on frequency of generalized tonic-clonic seizures (GTCS), atonic seizures (AS) and myoclonic seizures (MS) as they were the predominant types. In the CC group a significant reduction in the frequency of GTCS ($\geq 50\%$) was noted in 57% of patients, 50% showed significant reduction of AS (half of which were seizure free) and 29% of MS. In the VNS group 82% of patients had significant reduction of GTCS, 73% of AS (9% of which were seizure free) and 60% of MS (20% were seizure free).

Conclusion: Although the patient number in this study was relatively small, according to our results CC is not an inferior method in treatment of pharmacoresistant epilepsy with especially beneficial results on AS.

Disclosure: Nothing to disclose

EP1072

Frequency of post-stroke epileptiform activity - a systematic review and meta-analysis of observational studies

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Background and aims: Cerebrovascular disease is the most frequent risk factor for epilepsy, and epileptic phenomena following stroke are known to worsen prognosis. Electroencephalography (EEG) is the gold standard biomarker for epilepsy, but it is seldom used, and there is uncertainty about the frequency post stroke epileptiform activity as detected by EEG.

Methods: All studies indexed in MEDLINE, Embase, Web of Science, PsycINFO and OpenGrey (last search on March 2015), which reported the frequency of EEG epileptiform activity after stroke in adults were analysed. Epileptiform activity was defined as ictal activity (electroencephalographic seizures) and interictal activity (non-periodic spikes and sharp waves). Study selection, data extraction and risk of bias appraisal were performed by independent reviewers. Random-effects meta-analysis was used to pool frequencies. Prospero registration number: CRD42015029362.

Results: The electronic search was run on March 2015. A total of 2871 references were retrieved, and 18 studies were included. The pooled frequency of ictal and of interictal activity after stroke were 7% (95%CI 3%-12%) and 8% (95%CI 4%-13%), respectively. The use of continuous EEG did not change the frequency of ictal activity ($p=0.55$), nor did the management setting (ICU vs. non-ICU, $p=0.33$). However, studies with continuous EEG showed a greater frequency of interictal activity ($p=0.00$).

Conclusion: The frequency of ictal and interictal epileptiform activity was comparable, and consistent with previous analyses of clinical seizures. The former did not change with continuous record or clinical setting, while the latter increased with continuous record. Due to detection bias, it was not possible to correlate clinical and electroencephalographic seizures.

Disclosure: Nothing to disclose

EP1073

New peptide isolated from social wasp venom reduces neuronal cell death and spontaneous recurrent seizures after pilocarpine-induced status epilepticus

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Background and aims: Understanding the pathophysiology of temporal lobe epilepsy (TLE) largely rests on the use of models of status epilepticus (SE), like the pilocarpine model. After several hours of SE, pilocarpine-treated animals remit spontaneously and go into a seizure-free period, known as latent period, before displaying the spontaneous recurrent seizures (SRSs) that characterize the chronic epileptic condition. Based on this, the purpose of our study was to further characterize the capacity of neurovespina (a new peptide similar to one found in a social Brazilian wasp *Polybia occidentalis*) to prevent SRSs and hippocampal neuronal loss.

Methods: During chronic period (fifteen days after SE) animals (swiss mice, $n=7$) developed a chronic condition determined by SSRs and received daily intraperitoneal injections of neurovespina (doses: 1, 2 or 4 mg/Kg) or saline (control groups) to evaluate the behavioral effectiveness antiepileptic effect. The occurrence of seizures (Racine scale) was evaluated during two weeks (video recorded 9 hours/day).

Results: Our results showed that neurovespina reduced the score, time and number of SSRs in all doses when compared to control group and in the highest dose (4mg/Kg), animals have no seizure in the first 5 hours after treatment during all chronic period. Morphological analysis of hippocampal formation shows no significant loss of selective populations of interneurons in areas CA1 and CA3 and in the hilus.

Conclusion: These data indicate that Neurovespina has potential for the development of novel drugs for neurological diseases, both to reduce the seizures frequency and to minimize the neuronal damage associated with seizures.

Disclosure: This work was supported by FapDF and CNPQ.

EP1074

Cancelled

EP1075

Continuous thetaburst stimulation for the treatment of refractory neocortical epilepsy

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Background and aims: Repetitive transcranial magnetic stimulation may have anti-epileptic effects, especially in neocortical epilepsy. Continuous thetaburst stimulation (cTBS) seems to be a potent protocol that could optimize safety, tolerability and applicability based on lower stimulation intensity and shorter duration.

Methods: Patients with refractory neocortical epilepsy are treated with a 4-day accelerated cTBS protocol (figure 1) targeted over the epileptogenic focus. Seizure frequency and adverse events are assessed over a 4-week baseline period and 8 weeks of follow-up. Cognitive and psychological testing is performed at baseline and end of follow-up.

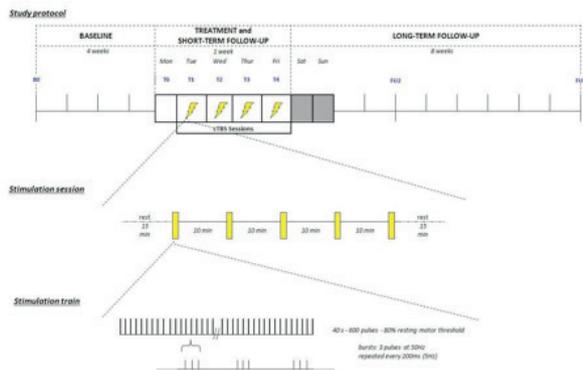


Figure 1: Overview of stimulation protocol

Results: Subject 1 and subject 2 suffer from epilepsy due to a low-grade tumor in the motor cortex causing focal clonic seizures. Subject 1 also experiences myoclonia of the left leg. Subject 3 has epilepsy with auditory seizures following intracranial hemorrhage in the left temporal lobe. cTBS was well-tolerated and did not induce serious adverse events or seizures. Mild headache occurred in subject 3. No negative cognitive or psychological side effects were noticed. Anti-epileptic effects of cTBS varied. Subject 1 experienced a transient reduction in severity of clonic seizures, with complete resolution of myoclonia for 6 weeks. Subject 2 experienced an overall 50% seizure frequency reduction, with most pronounced effect during treatment and initial 4

weeks of follow-up (70% reduction, 3 seizure-free weeks). No marked effect on seizures was identified in subject 3.

Conclusion: cTBS appears safe and well-tolerated, even in seizure-prone subjects. Anti-epileptic effects of variable extent were identified. Extensive parenchymal damage at the target site may have interfered with effective stimulation in subject 3.

Disclosure: Nothing to disclose

EP1076

MERRF presenting with drop attacks due to astatic epileptic crises

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Background and aims: Mitochondrial encephalopathy with ragged red fibers (MERRF) is a progressive mitochondrial disorder characterized by myoclonus, epilepsy, ataxia and myopathy. Drop attacks are seldom recognized as a feature of MERRF.

Methods: A clinical case.

Results: A 50-year-old male presented to our clinic complaining of repetitive drop attacks. He claimed periodic loss of muscle tone in his lower limbs, with loss of orthostatic posture, without impaired consciousness or trigger. The episodes started 10 years earlier and had worsened, occurring now nearly on a daily basis. His previous medical records were remarkable for Wolf-Parkinson-White syndrome, auditory and visual impairment, and surgical removal of neck lipomas. His parents were non-consanguineous. His brother had similar events. His neurological examination was striking for mild cognitive impairment, slow and segmented saccades with limited upgaze, bilateral ptosis, dysarthria, mild proximal muscular weakness, distal hypoesthesia in the lower limbs, diminished reflexes and a wide-based unstable gait. The diagnostic work-up revealed: elevated CK (~1000IU/L); axonal sensory-motor polyneuropathy; bilateral neurosensory hearing loss; generalized cortical atrophy (MRI); abundant bilateral frontotemporal delta rhythm, without paroxysmal activity detected on EEG. Empirical levetiracetam was started, with near-total remission of the astatic crises. MERRF was suspected and a mutation in the MT-TK gene was found confirming the diagnosis.

Conclusion: We describe a case of MERRF presenting with drop attacks due to astatic/tonic epileptic events and excellent improvement with levetiracetam. Multisystemic dysfunction with combination of either: epilepsy, cerebellar, visual or auditory impairment, neuropathy, myopathy, cardiac abnormalities and midline lipomas should raise suspicion of this entity.

Disclosure: Nothing to disclose

EP1077

Cancelled

Headache and pain 1

EP1078

The effects of OnabotulinumtoxinA treatment on the chronic migraine comorbidities of sleep and fatigue

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Background and aims: Chronic migraine (CM) is associated with comorbidities that may exacerbate the condition. This subanalysis of COMPEL addresses effects of onabotulinumtoxinA prophylaxis on comorbid sleep disturbances and fatigue symptoms.

Methods: The 108-week, multicentre, open-label COMPEL Study enrolled adult patients with CM in Australia, Korea and the United States receiving onabotulinumtoxinA 155 U with/without concomitant prophylaxis. Primary outcome was reduction in headache frequency per 28-day period at 108 weeks (9 treatments). Sleep disturbances were assessed using the Pittsburgh Sleep Quality Index (PSQI) and fatigue symptoms using the Fatigue Severity Scale (FSS). Adverse events (AEs) were recorded.

Results: Enrolled patients (N=715) had a mean (range) age of 43 (18-73) years and were predominantly female (84.8%, 606/715). Headache day frequency at week 108 (primary endpoint) was significantly reduced from a baseline mean (standard deviation, SD) of 22 (± 4.8) days to 10.7 (± 6.4) days ($P < 0.0001$). Patient baseline mean (SD) PSQI score was 13.3 (± 3.7), which indicated poor sleep quality. OnabotulinumtoxinA treatment significantly improved PSQI mean scores at weeks 24, 60, 84, and 108 (all $P < 0.0001$; Figure 1). Baseline mean FSS score of 38.1 (± 14.5) was also significantly improved at all time points ($P < 0.0001$; Figure 2). Most AEs were mild or moderate in nature; low rates of treatment-related AEs were observed (Table).

Figure 1. Mean Total PSQI Scores and Decreases from Baseline by Visit

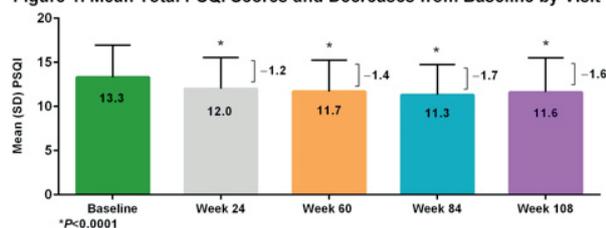


Figure 2. Mean Total FSS Scores and Decreases from Baseline by Visit

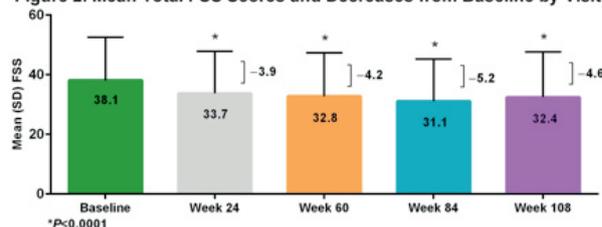


Table. Treatment-Related Adverse Events

Event, n (%)	Overall (N=716)
Neck pain	29 (4.1)
Eyelid ptosis	18 (2.5)
Musculoskeletal stiffness	17 (2.4)
Injection site pain	14 (2.0)
Headache	12 (1.7)
Muscular weakness	10 (1.4)
Facial paresis	9 (1.3)
Migraine	7 (1.0)
Skin tightness	7 (1.0)

Conclusion: Results from the COMPEL Study indicate the effectiveness of onabotulinumtoxinA treatment for reducing headache frequency as well as improving sleep quality and fatigue symptoms up to 108 weeks (9 treatment cycles) in patients with CM. No unexpected AEs were reported.

Disclosure: The funding source for this study is Allergan plc (Dublin, Ireland)

EP1079

SUNCT/SUNA syndrome with cardiac symptoms

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Background and aims: Case report of a short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms (SUNA) syndrome with transient atrioventricular block during attacks.

Methods: Female, 39-year-old, affected by arterial hypertension and benign familial hematuria, no history of syncope or headaches, was admitted to the hospital presenting episodes of severe burning facial pain affecting left nasal and maxillary, shorter than one minute, with ipsilateral tearing and nasal congestion, dizziness and one syncope. During her stay in emergency room she suffers new episode, with syncope. Electrocardiography monitoring showed complete atrioventricular (AV) block during attack, nodal rhythm at 20 beats a minute, spontaneously recovered to normal sinus rhythm. Normal physical exam. The patient was admitted to Intensive Care Unit, persisting attacks with AV block: an external pacemaker was necessary, changed later by a definitive pacemaker.

Results: A cranial tomography (CT) scan showed left cerebellar hemisphere hypodensity, confirmed as chronic left cerebellar infarction by magnetic resonance (asymptomatic). Etiological studies for stroke (CT angiography, hypercoagulability tests, echocardiography) were negative or normal. Indomethacin obtained pain control; lamotrigine rising dose was indicated in order to indomethacin withdrawal, no more episodes with 400mg per day.

Conclusion: SUNA syndrome is a quite unusual headache classified into a group of primary headaches called trigeminal autonomic cephalalgias. Diagnosis features of the group includes unilateral pain and local parasympathetic autonomic symptoms. This is the only case in literature in which pain attacks associate AV block, suggesting hyperactivity of the parasympathetic pathway that exceed local response. Left cerebellar infarction could play an etiological role.

Disclosure: Nothing to disclose

EP1080

Aphasic aura and reversible MRI image in hemiplegic migraine

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Background and aims: Familial Hemiplegic Migraine (FHM) is defined by the occurrence of hemiparesis as part of the aura (ICHD-3 Beta). One of the differential diagnosis is an ischemic stroke. We report a case of FHM that was studied during a prolonged migraine attack.

Results: A 29-year-old woman, developed an intense headache, associated with aphasia and right hemiparesis. She has been diagnosed with FHM type 2 years before with T376M mutation of ATP1A2 gene, localized in 1q21-23 chromosome. Weakness recovered in 24 hours, but she persisted with an atypical aphasia with fluctuating degree of fluency, ranging from periods of almost no speech or difficulty initiating speech to others of fluent speech with paraphasias. Cranial MRI showed a left cortical hypersignal on the temporo-parietal lobe and cingulate gyrus on FLAIR but not on DWI. There were no ischemic lesions. EEG showed no paroxysmal activity. The patient recovered from the aphasia in one month, and she repeated the MRI that was normal.

Conclusion: The aura phenomenon has been attributed to cortical spreading depression with vasogenic edema. In this case, the parallel course of symptoms and reversible vasogenic edema supports this pathogenesis. The language disorder was rather atypical for a stroke aphasia, suggesting that the functional impairment is not fixed. This case has unusual features because changes were only observed in FLAIR which is unusual in FHM, where most cases have changes in DWI/FLAIR. The negative DWI excludes ischemic stroke, but FLAIR showed a cortical edema, lead to think in other causes, like FHM.

Disclosure: Nothing to disclose

EP1081

Headache linked to intracranial hypertension and hypertrophic pachymeningitis as the initial and dominant presentation of Granulomatosis with polyangiitis (Wegener granulomatosis)

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Background and aims: Granulomatosis with polyangiitis (GPA, or Wegener granulomatosis) is a rare, systemic disease of unknown etiology, characterized by necrotizing granulomatous inflammation and systemic vasculitis. We are reporting a case of patient with headache as the presenting symptom.

Methods: A 54-year-old male, without any related medical history, developed a non-specific, severe and unresponsive to various treatments headache. In the following 2 months, he gradually developed hoarseness and diplopia affecting the left abducens nerve. An ophthalmological examination revealed bilateral papilledema and diffused flame-like retinal hemorrhages, implying the presence of intracranial hypertension. A brain MRI revealed wide-spread fattening and meningeal enhancement of the left hemisphere, and also mild swelling and inhomogeneous signal at the left half of the nasopharynx. An endoscopy of the pharynx revealed the presence of a tumor-like mass in the left half of the nasopharynx. A biopsy showed inflammation with presence of polykaryocyte Langhans giant cells, implying a specialized granulomatous inflammation. The laboratory testing revealed important albuminuria and microhematuria, positive c-ANCA and negative p-ANCA.

Results: Having fulfilled three out of four diagnostic criteria of the American College of Rheumatology for GPA, we initiated a steroid treatment with a drastic improvement of headache. During the following weeks, the remaining symptomatology resolved gradually whereas a follow-up brain MRI showed a decrease in meningeal enhancement.

Conclusion: Participation of the central nervous system at the initial stage of GPA is an extremely rare condition and occurs in up to 8% of patients. Headache as the sole presenting symptom of GPA is additionally rare and may elude early diagnosis.

Disclosure: Nothing to disclose

EP1082

Migraine and autoimmunity: How often are autoimmune disorders reported by headache patients

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Background and aims: Although the pathophysiology of migraine is not yet totally understood, a possible role of immunological dysfunction and/or autoimmunity has been reported. The aim of this study was to analyse the frequency of autoimmune disease reported by migraine patients and patients with non-migraine headache.

Methods: We review the clinical files of consecutive patients observed in our Headache Ambulatory Clinic between January 2013 and December 2015. Demographic and clinical data, including all the information regarding any diagnostic of autoimmune disorder, were collected. Diagnosis of headache was made based on ICHD3-beta criteria. Migraineurs and patients with headache without migraine features were compared on frequency of the diagnosis of autoimmune disorders. SPSS was used for statistic analysis and a p value of <0.05 was considered significant.

Results: 433 patients, 85% female, median age 43 years (18-92, min-max), 279 (64%) with migraine. Autoimmune disease were reported by 28 (6,5%) patients, 22 (8,6%) migraineurs and 6 (4%) non-migraneurs (p=0,106). Inflammatory Bowel Disease (6 patients), Systemic lupus erythematosus (4) and Psoriasis (4) were the most frequent autoimmune disorders reported. Patients with autoantibodies but without diagnosis were not considered as having autoimmune disease.

Conclusion: In our cohort we didn't find a significantly greater prevalence of autoimmune disorders in migraine patients than in patients with other headache types. Studies with more patients with structured questionnaires regarding autoimmune symptoms and conditions, could help clarify the role of autoimmunity in migraine.

Disclosure: Nothing to disclose

EP1083

Acute Hashimoto's Thyroiditis presenting as worsening of migraine without aura

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Background and aims: The prevalence of hypothyroidism in migraine is significantly higher than in the general population. Hypothyroidism should be considered as one of the variety of migraine comorbidities, even if possible pathophysiologic relationships remain unclear. Presenting an interesting case of autoimmune thyroiditis which was detected during acute phase of migraine.

Methods: Case Study

Presenting young 22-year-old lady, known case of migraine diagnosed 6 years back on regular prophylaxis came with acute headaches, holocranial, throbbing in character, associated with vomitings and nausea and photophobia, no preceding aura, partially relieved with analgesics. Examination showed conscious cooperative, dull, apathetic, no localising deficit, vitals normal CTSCAN HEAD Normal, blood biochemistry normal, CBC normochromic normocytic anaemia, T4 low, TSH high and anti TPO 1008IU/ml, Patient started on intravenous fluids, analgesics, steroids and thyroxine. Gradually patient improved.

Results: This is the first case report of migraine without aura getting worse secondary to auto immune thyroiditis. it is proposed that antibodies primary directed against the thyroid gland, “leak” across the blood-brain barrier into the brain parenchyma, inducing an autoimmune lymphocytic response based on shared antigens between brain and thyroid.

Conclusion: Headache disorders may be associated with an increased risk for the development of new onset hypothyroidism. Auto immune thyroiditis can affect from headaches, seizures, and steroid responsive encephalopathy, and early diagnosis helps in managing the patient efficiently.

Disclosure: NO GRANT

EP1084

A systematic literature review and meta-analysis of epidemiologic studies in chronic and episodic migraine

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Background and aims: Despite its public health importance, there is limited understanding on the epidemiology of migraine, especially regarding its demographic or geographic variation. International consensus on the definition of migraine has evolved over time contributing to heterogeneity seen across studies. This study aimed to systematically identify population-based studies that report prevalence and/or incidence of migraine in the past decade.

Methods: A systematic literature review (SLR) was conducted following the 2015 Preferred Reporting Items for Systematic review and Meta-Analysis Protocols (PRISMA-P). The search focused on English publications of population-based studies on the adult prevalence or incidence of migraine, chronic (CM) and episodic migraine (EM), published between 2006–2016. Sources searched were: Medline, EMBASE and conference proceedings (2014-2016) from the American Academy of Neurology, European Academy of Neurology, and International Headache Society. Information was extracted by two researchers independently in parallel and any disagreements were resolved by discussion or independent arbitration by a third reviewer.

Results: 1047 publications were retrieved in total (128 of those were identified from conference abstracts, 915 from database searches and 4 from previously published SLRs or meta-analyses). Overall, 56 publications corresponding to 37 unique studies were retrieved (Figure 1). Fifty-five publications reported prevalence and 1 reported incidence only. The 1-year prevalence of migraine ranged from 4.3% to 45.5%.



Figure 1. PRISMA Diagram for the Systematic Literature Review of Epidemiologic Studies in Migraine

Conclusion: Limited availability of epidemiological estimates in migraine exists. This SLR provides a systematic summary of the available population-based studies reporting prevalence of migraine in the last decade which can form the basis of subsequent meta-analysis for subgroups of interest

Disclosure: This study was sponsored by Novartis Pharma AG, Basel, Switzerland

EP1085

Association of migraines with suicidal ideation among immigrants: Experience of the emergency department of a Greek Tertiary Clinic

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Background and aims: Suicide represents a significant global public health and social concern, and suicide rates have been increased in patients with migraine. Immigrant and ethno-cultural minorities face mental health challenges associated with suicide behaviours, however, data on pain-associated suicidality are lacking. Our aim was to investigate a potential link between migraine and suicidal ideation among immigrants.

Methods: We conducted a retrospective study of all visits in our emergency department between 2014-2016. All immigrants completed the questionnaires, including demographics, headaches characteristics, depression and suicidal ideation (Patient Health Questionnaire9). Diagnoses of headaches were made according to International Classification of Headache Disorders-III beta criteria. Multivariable logistic regression analyses were performed to estimate odds ratios (OR) and 95% confidence intervals (95% CI).

Results: Immigrants represent 22.6% (n=205) of the total number of visits because of headaches (n=5988). Migraineurs reported a higher frequency of suicidal ideation (16.1% [OR]=2.9, 95%[CI] 2.3-3.6; p<0.001), compared of non migraineurs. After controlling for depression score and sociodemographic characteristics, immigrants with migraine had 68% increased odds of suicidal ideation (OR=1.68; 95% CI: 1.36-2.17) compared with non-migraineurs. Women with migraine and depression were 2fold more likely to report suicidal ideation [OR =2.46, 95% CI (2.55- 4,46)]

Conclusion: Migraine is associated with increased likelihood of suicidal ideation in immigrants after adjusting for depression. These findings may further support the need to enforce health authorities for outpatient management for this vulnerable population.

Disclosure: Nothing to disclose

EP1086

Stroke-like migraine attacks after radiation therapy (SMART) syndrome with cerebrospinal fluid pleocytosis

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Background and aims: SMART syndrome is a rare syndrome characterized by a remote history of cranial irradiation, severe headache and seizures with prolonged and reversible neurological signs and symptoms referable to a unilateral cortical region. The diagnosis relies on brain MRI and exclusion of alternative diagnoses. Cerebrospinal fluid (CSF) analysis is usually inconclusive.

Methods: Case report

Results: Eighteen-year-old male was diagnosed with glioblastoma of the right frontal lobe in 2008 (age of 10). After the surgery he was treated with chemo- and radiotherapy (59.4Gy) and recovered completely.

In April 2016 he experienced a migraine like headache with numbness and weakness of the left upper limb which spontaneously subsided after 10 minutes. A week later he suffered a severe throbbing headache and paresis of the left upper limb after a night of partying and drinking alcohol. Over 14 days left-sided hemiplegia with left hemispatial neglect and hemianopsia evolved. He suffered several generalized seizures. MRI revealed cortical enhancement over the right hemisphere with spared white matter (Figure 1). CSF analysis revealed pleocytosis (white blood cells count of 12×10^6 with 6×10^6 neutrophils, 4×10^6 lymphocytes and 2×10^6 monocytes). Extensive tests performed to exclude infectious causes were negative. After treatment with verapamil, nimodipine and dexamethasone neurological deficits and headache subsided completely over 8 weeks. Follow up MRI after 7 months showed complete regression. CSF pleocytosis also subsided.

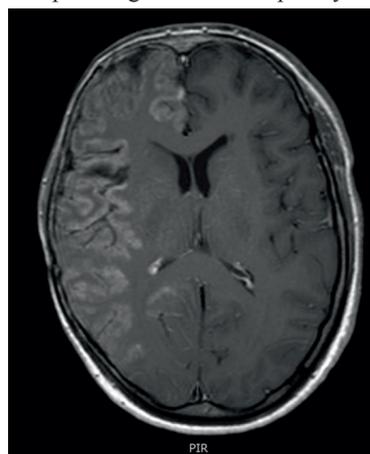


Figure 1: MRI showing vast involvement of the right cerebral hemisphere with no tumor recurrence.

Conclusion: This is the first report of SMART syndrome with CSF pleocytosis. Additionally we speculate that ethanol with its effect on endothelial function might provoke development of the SMART syndrome.

Disclosure: Nothing to disclose

EP1087

Psychometric properties of brief pain inventory for assessing hemiplegic shoulder pain

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Background and aims: Hemiplegic shoulder pain (HSP) affects up to 84% of stroke patients and potentially impacts daily functions for stroke patients. However, no scale has yet been developed specifically for HSP. Brief Pain Inventory (BPI) short form is common to evaluate the worst pain intensity (BPI3) and pain interference in daily life (BPI9). The purpose of this study is to investigate psychometric properties of the BPI for assessing HSP.

Methods: Eighty stroke patients were recruited to rate shoulder pain twice, at one-week interval, with BPI and Numerical Rating Scale (NRS). The NRS was used as comparator with BPI to examine concurrent validity using Spearman's rho correlation coefficient (ρ). Test-retest reliability of BPI was analyzed with the intraclass correlation coefficient (ICC) for determining the degree of consistency and agreement between test-retest. The standard error of measurement (SEM), minimal detectable change (MDC), Bland-Altman limits of agreement (LOA) were the absolute reliability indexes used to quantify measurement errors and determine systematic biases of repeated measurements.

Results: Concurrent validity of the BPI was moderate ($\rho=0.62-0.72$). The ICCs of the BPI3 and BPI9 were 0.88 and 0.86. The SEMs of BPI3 and BPI9 were 0.99 and 0.57. The MDC95 of the BPI3 and BPI9 were 2.74 and 1.58. The Bland-Altman analyses revealed no significant systematic bias between repeated measurements and narrow range of the LOA for the BPI indicated a high level of stability.

Conclusion: The BPI demonstrated good concurrent validity and reliability for measuring shoulder pain in stroke patients.

Disclosure: This work was supported by the Ministry of Science and Technology (104-2314-B-182-035-MY3) and Chang Gung Memorial Hospital (CMRPD3E0331) in Taiwan.

EP1088

Cancelled

EP1089

Cancelled

EP1090

Myofascial pain and musculoskeletal dysfunction

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Background and aims: Myofascial trigger zone [TrZ] are a common cause of musculoskeletal pain. The aim of this study was to evaluate the mechanisms of myofascial TrZ formation and to reveal possible changes in muscle ultrastructure related to myofascial pain syndrome.

Methods: Thirty-six patients with myofascial pain syndrome, mean age 38.4 years (SD 9.7), and 12 age-matched controls were included in this study. The trapezius and brachioradialis muscles were examined by means of single fiber and concentric needle electrodes and electron microscope.

Results: Electrophysiologic studies have revealed significant changes in the shape of the main spike motor unit and endplate potentials: decrease in the duration and amplitude of motor unit potentials, increase in the duration and rise time endplate potentials in myofascial TrZ. The fiber density was increased and mean jitter higher in the TrZ than in control group. The destruction of contractile apparatus involves myofibrils loss and broadened interfibrillar distance. In some parts of muscle we observed total destruction of several sarcomeres. Structure of Z-lines was changed significantly. Autophagosomes in the peripheral part of the cell in sarcoplasm near cellular nucleus were found.

Conclusion: The neuromuscular dysfunction in the immediate vicinity of a motor endplate is the anatomical substrate of TrZ, which produced typical characteristic electrical activity. Divergence of myofilaments and Z-line can be associated with cytoskeletal protein destruction. The presence of autophagosomes associates either with breach of neurotrophic control or with muscle atrophy after exhausting physical activity. All this can be the basis of effective therapy in patients with myofascial pain syndrome.

Disclosure: Nothing to disclose

EP1091

Cancelled

Infection and AIDS

EP1092

Central nervous system infection with *Listeria monocytogenes*: 20 years experience in a tertiary hospital

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Background and aims: *Listeria monocytogenes* (Lm) is the third leading cause of bacteria central nervous system (CNS) infection; it especially affects immunosuppressed patients. We present the largest series of patients with CNS involvement by Lm of a Spanish hospital. We analyzed the risk factors for the development of CNS infection, temporal changes in incidence, presentation symptoms, cytopathological features of cerebrospinal fluid, radiological findings, treatment and prognosis.

Methods: Descriptive and analytical research of all Lm isolates collected prospectively by the Microbiology Unit in a tertiary hospital between January 1996 and May 2016.

Results: Lm was isolated in 104 patients, 44 had CNS involvement. There was an increase in the incidence of Listeriosis and CNS infection between 2006 and 2016, compared to the previous decade. CNS infection was associated with treatment with immunosuppressive drugs. The most frequent presenting symptoms were fever and impaired awareness. 27% of patients presented with rhombencephalitis. There was a case of brain abscesses. 73% of patients healed without sequelae. Mortality (11%) was only associated with neoplasms. The majority of patients were treated with ampicillin and gentamicin, with no differences in mortality compared to other therapeutic regimens.

Conclusion: The incidence of CNS infection with Lm has increased in recent years, associated with immunosuppressive treatments and neoplasias. The overall mortality rate was low, with no differences according to the antibiotic treatment used.

Disclosure: Nothing to disclose

EP1093

First case reported of cytomegalovirus encephalitis in a multiple sclerosis patient in treatment with fingolimod

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Background and aims: Cytomegalovirus (CMV) encephalitis is an important opportunistic infection that occurs in HIV patients, especially in patients with CD4 <50/mm³, but is rarely recognized in other groups. We present a case of CMV encephalitis in a patient in treatment with fingolimod for multiple sclerosis (MS).

Methods: 22-year-old woman diagnosed of MS since 19-years-old. In treatment with fingolimod with a lymphocyte count always >200/mm³. She has a medical history of Hodgkin lymphoma (in complete remission since 17-year-old) and migraine with aura. The patient presented in the emergency department (ED) with a severe migraine crisis with prolonged aura. Later began with altered level of consciousness, aggressive behaviour and altered speech. At examination was afebrile. Brain CT, basic blood test and lumbar puncture were performed,

Results: Blood lymphocyte count was 60/mm³ (previous week 380/mm³). We began treatment with aciclovir, suspended fingolimod and solicited DNA detection for herpesviridae despite brain CT and CSF composition were unremarkable and no fever. The patient recovered normal status progressively. CMV DNA was detected in CSF and treatment was switched to galanciclovir i.v and then to valaciclovir p.o. Brain MRI didn't show any new alterations. This would be the first case described of CMV encephalitis in patients with multiple sclerosis treated with fingolimod, since we did not find any publication after a bibliographic search. In cases of encephalopathy in an immunocompromised patient (regardless of the cause), CMV encephalitis should be suspected even in the absence of fever, cerebrospinal fluid composition and neuroimaging without alterations.

Disclosure: Nothing to disclose

EP1094

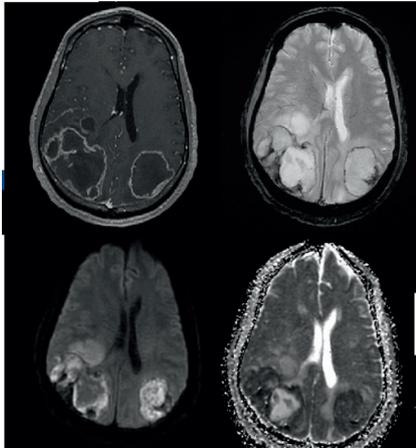
Central nervous system histoplasmosis due to *histoplasma capsulatum* var. *duboisii*: First case report and literature review

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Background and aims: Histoplasmosis is a disease caused by the fungus *Histoplasma capsulatum* whom two different varieties exist: *Histoplasma capsulatum* var. *capsulatum* (American histoplasmosis) and *Histoplasma capsulatum* var. *duboisii* (African histoplasmosis). Central nervous system involvement in the *Duboisii* variety as never been reported yet, we report a case.

Methods: We report a 47-year-old man from Congo, who has lived in France for twenty years and recently travelled to Congo, with a picture of cognitive impairment rapidly installed in a few months. The only localising sign was a left homonymous hemianopsia. There was no extra-neurological sign or symptoms. He was afebrile and laboratory results were normal. Brain magnetic resonance imaging revealed bilateral parieto-occipital ring-enhancing brain lesions. Stereotactic-guide cerebral biopsy was performed and revealed yeasts of *Histoplasma capsulatum* var. *duboisii* on direct examination confirmed by polymerase chain reaction-sequencing. The complementary work-up revealed no immunodeficiency and asymptomatic pulmonary and ocular localisation. The treatment is ongoing with amphotericin B and switch to oral itraconazole. We searched PubMed® from inception to december 2016 to identify case reports of cerebral histoplasmosis involving *histoplasma duboisii*.



Brain magnetic resonance imaging revealed bilateral parieto-occipital ring-enhancing brain lesions

Results: A total of 105 case reports of *histoplasma duboisii* infection were identified. Localisations reported were cutaneous, bone, pulmonary, lymphadenic, digestive and one adrenal glands. No cerebral histoplasmosis involving the *duboisii* variety was reported.

Conclusion: Histoplasmosis is a rare cause of brain tumor-like clinical and radiological picture which has been reported in American Histoplasmosis. Central nervous system involvement in the *Duboisii* variety has never been reported yet, we report a case.

Disclosure: Nothing to disclose

EP1095

Acute measles encephalitis with an atypical clinical presentation in a vaccinated adult

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Background and aims: Despite the availability of an effective vaccine, measles remains a leading cause of death among children in developing countries. While unvaccinated children are at highest risk of infection and its complications, they can occur even in vaccinated patients. Neurological complications may occur early (acute postinfectious encephalitis) or after years of viral persistence (subacute sclerosing panencephalitis).

Methods: Case report.

Results: A 19-year-old female patient was diagnosed with a right eye retinitis and started treatment with oral methylprednisolone during 20 days. She had no relevant previous medical history and previously received measles vaccination. Five days after the suspension of corticotherapy, she rapidly developed progressive behavioural changes, global aphasia, right hemiparesis and right homonymous hemianopsia. CSF study revealed mild mononuclear pleocytosis. Brain MRI showed bilateral temporal pole and left temporo-parieto-occipital T2 hyperintensities. EEG revealed a pattern of left hemispheric slowing without periodic complexes or paroxistic activity. Metabolic, immunological, bacteriological and viral studies, as well as the search for paraneoplastic syndromes were negative. She continued having a clinical, imagiological and electroencephalographic worsening without response to antivirals or immunotherapies that included high dosage corticotherapy, plasmapheresis and cyclophosphamide. Brain biopsy revealed intranuclear inclusions in oligodendrocytes compatible with paramyxovirus nucleocapsids. The patient became fully dependent and died a year later due to an infectious complication.

Conclusion: This case illustrates a severe atypical presentation of measles encephalitis occurring in a previously healthy vaccinated patient. While the absence of rash history raises some doubts regarding the moment of primary infection, we propose that the retinitis may have corresponded to the primary infection.

Disclosure: Nothing to disclose

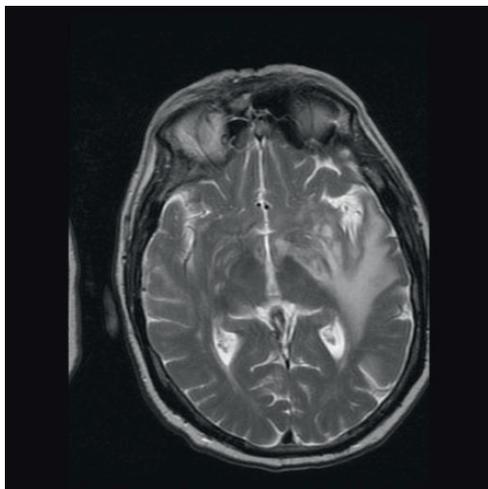
EP1096

Cognitive impairment of the frontotemporal profile as a debut of Whipple's disease

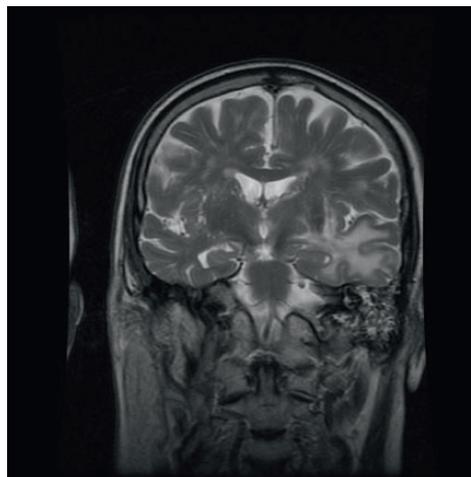
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Background and aims: Neurological Whipple's disease without previous systemic involvement is not frequent but can have different clinical presentations. In this way we present an atypical case with frontotemporal dementia syndrome and pseudotumoral neuroimaging.

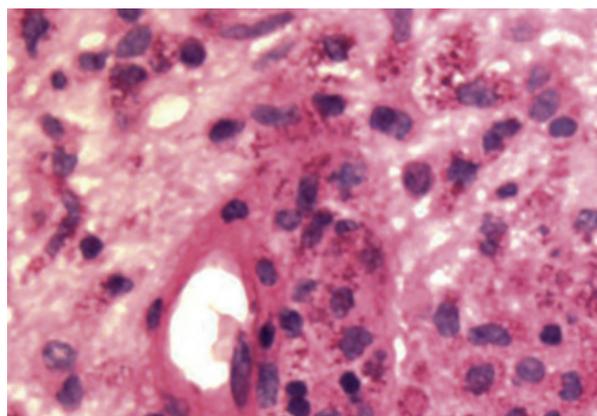
Methods: A 71-year-old male with a 3-month history characterized by mnemonic failures and deliriform thought that weeks later had dysphasic language with semantic paraphasias, dysnomia, inability to understand complex orders, confusion between right-left, loss of executive skills and apathy. In cranial MRI (magnetic resonance imaging) presented an extensive lesion in the left temporal region that resembles a high grade glioma. Given this finding and the nonspecific nature of the lesion, a cerebral biopsy was performed reporting the presence of intracytoplasmic inclusions and bacilliform structures free in the neuropilo, compatible with the diagnosis of encephalitis by *Tropheryma Whipplei*, confirmed with positive PCR (Polymerase Chain Reaction) in brain tissue.



Lesion in the left medial temporal region



Lesion in the left medial temporal region



Brain tissue with intracytoplasmic inclusions and bacilliform structures

Results: This clinical case refers a patient with a frontotemporal dementia as a unique clinical manifestation of Whipple's disease, with no prior intestinal involvement, ruled out by duodenal biopsy, which needed three years of antibiotic treatment with ceftriaxone and trimetoprim/sulfamethoxazole. He currently presents radiological and clinical stability after five years of follow-up.

Conclusion: Our case is exceptional because it shows a patient with Whipple's disease that begins with cognitive affectionation with a pseudotumoral neuroimagen without a history of intestinal or systemic infection.

Disclosure: Nothing to disclose

EP1097

Clinical manifestation and treatment outcome of Parvovirus B19 encephalitis in immunocompetent adults

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Background and aims: Since human parvovirus B19 (PVB19) was discovered from the serum sample of a normal blood donor in the mid-1970s, its infection has been reported to cause a variety of clinical manifestations, such as erythema infectiosum, transient aplastic crisis, non-immune hydrops fetalis, and arthritis. PVB19 has rarely been identified as a cause of encephalitis in immunocompetent adults, in whom clinical information regarding PVB19 encephalitis has remained unclear.

Methods: We reviewed a series of consecutive patients with acute encephalitis who underwent extensive workups for pathogens in the serum and cerebrospinal fluid (CSF) between May 2006 and May 2016 at Seoul National University Hospital. We included patients older than 18 years who had positive PVB19-polymerase chain reaction (PCR) results from their serum or CSF samples.

Results: Although none of the patients showed any distinctive features of PVB19 infection, they showed various clinical manifestations, including one instance of brainstem involvement. Seizure was an especially frequent symptom, which was well controlled with antiepileptic drugs. All the patients showed favorable outcomes at discharge. However, two received immunotherapy due to insufficient recovery from the antiviral treatment; subsequently, these patients showed remarkable improvement.

Conclusion: PVB19 infection should be considered as a possible cause of acute encephalitis syndrome in immunocompetent adults. Since the clinical presentation of PVB19 encephalitis in immunocompetent adults generally shows a favorable outcome, and immunotherapy can be considered a treatment option, especially in those who are resistant to the initial management.

Disclosure: Nothing to disclose

EP1098

Clinical presentation and diagnostics of Lyme neuroborreliosis in the period of 2005–2015 at the department of neurology in Vilnius, Lithuania

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Background and aims: Lyme neuroborreliosis (LNB) is a tick-borne neuroinfection caused by spirochete *Borrelia*. Our aim of the study was to analyse seasonal variation, symptoms and diagnostics of LNB.

Methods: The medical records of 91 patients with confirmed LNB, who were hospitalized at the Department of Neurology, Vilnius University Santariskiu Clinics, Lithuania, in the period from 4 September 2005 to 4 September 2015 were analysed. The diagnosis of definite/possible LNB was made according to EFNS guidelines on the diagnosis and management of European Lyme neuroborreliosis.

Results: The mean age was 49±17 years, the male/female ratio was 48/43. One third of the patients had a history of a tick bite, only 10% erythema migrans. The mean annual rate of LNB varied significantly (highest rates in 2009, 2010, 2012, 2014). Most of the LNB cases occurred in summer and autumn, but 15% of all cases occurred in winter-spring season. Bannwarth's syndrome was the most common (47%) clinical presentation, meningoencephalitis (24%) and meningitis (21%) were frequent also. Mean cytosin - 174 cells per mm³ (median: 104), mean protein concentration 1,22g/l (median: 0,96). 91% of the patients had positive anti-B.burgdorferi (anti-BB) antibodies test from blood serum or cerebrospinal fluid. 12% had positive anti-Tick-borne-encephalitis-virus antibodies.

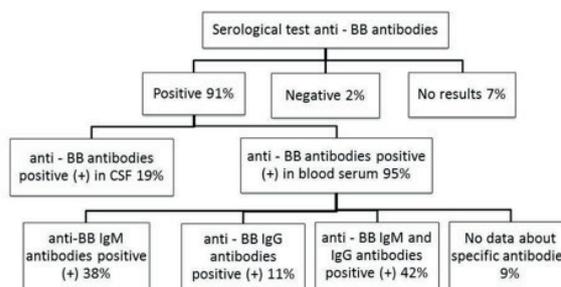


Table 1. Serological test results of anti-BB antibodies.

Conclusion: LNB is highly seasonal disease though some of the cases occur in winter and spring. The most common clinical presentation is Bannwarth's syndrome and meningoencephalitis. The co-infection with Tick-borne-encephalitis virus must be considered.

Disclosure: Nothing to disclose

EP1099

A multi-centre audit of the management of HSV encephalitis in the North West of England

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Background and aims: Herpes Simplex Virus (HSV) encephalitis is a severe, potentially fatal infection of the brain parenchyma affecting between 1 in 250,000 and 1 in 500,000 each year. Prognosis has been historically poor, but the early institution of therapy can improve outcomes.

We audit the management of patients across two hospital trusts; encompassing a Neurosciences centre, Infectious Diseases centre and two District Generals.

Methods: Patients with PCR positive CSF results for HSV-1 and HSV-2 were identified and cross-referenced with those clinically coded as meningoencephalitis within a 1-2 year period. Records were audited according to the 2012 guidance.

Results: A total of 16 patients were included, (n=10 male, n=6 female) with average age at presentation 63 years. Patients presented with decreased GCS (n=10), headache (n=6), seizure (n=5), collapse (n=3) and focal neurology (n=2). Clinical suspicion of encephalitis was documented on average 32 hours after initial presentation. CT brain was completed in 81% of patients, on average 26.5 hours following initial presentation and 69% of patients underwent MRI brain. Lumbar puncture was performed in 93.8% of patients, on average 16.5 hours following documented suspicion. HSV was identified by PCR in 75% of cases. Acyclovir therapy was commenced in 94% of patients, on average 32 hours after initial presentation. Acyclovir was stopped following negative CSF PCR in 69%, due to clinical improvement in 23% and following self-discharge in 7% of patients.

Conclusion: This study continues to identify delays in diagnosis, investigation and the initiation of therapy but also highlights a disparity regarding the decision to stop acyclovir therapy.

Disclosure: Nothing to disclose

EP1100

Neurobrucellosis: A case of reversible rapidly progressive dementia

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Background and aims: Portugal is considered a high risk country for brucellosis. About 5% of the cases develop neurobrucellosis with heterogeneous manifestations, usually accompanied by CSF lymphocytic pleocytosis.

Methods: Case Report

Results: A 81-year-old female was admitted to the neurology ward for rapidly progressive cognitive impairment and frequent falls, causing complete dependency for activities of daily living in 4 months. The patient was afebrile, alert, disoriented with incoherent speech, presented with bilateral extrapyramidal signs and was unable to walk. Head CT and MRI revealed bilateral hippocampal atrophy and moderate leukoaraiosis. CSF analysis showed lymphocytic pleocytosis (25 cells/uL), hyperproteinorraquia and hypoglucoorraquia. Despite the absence of relevant epidemiological history, both serum tube agglutination test and CSF polymerase chain reaction (PCR) were positive for Brucella. The patient was started on trimethoprim/sulfamethoxazole, doxycycline and rifampicin and discharged after 2 months, partly improved. Three weeks later, she was readmitted due to persistent CSF pleocytosis and trimethoprim/sulfamethoxazole was changed to ceftriaxone. After 3 months, the patient was discharged on trimethoprim/sulfamethoxazole, doxycycline and rifampicin. After completing 9 months of antibiotic therapy, CSF normalized, extrapyramidal signs disappeared, her gait was normal and she had autonomy for most activities of daily living.

Conclusion: In this case, some clinical and imagiological elements could suggest a neurodegenerative etiology. However, its rapidly progressive course requires exclusion of potentially reversible causes of dementia. Neurobrucellosis is a treatable cause of recent cognitive impairment, requiring prolonged antibiotic therapy, and should be considered in the presence of CSF lymphocytic pleocytosis even without fever or suggestive epidemiological context.

Disclosure: Nothing to disclose

EP1101

Increasing proportion of HIV infection in patients with stroke over a period of 16 years in Spain

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Background and aims: An increase of the incidence of stroke in HIV patients has been reported in recent years. We assessed trends in proportion of HIV infection among patients with stroke in Spain.

Methods: Data were obtained from the national minimum basic dataset. All patients hospitalized between 1997 and 2012 with a diagnosis of stroke at discharge were included. Annual proportion of HIV infection and time trends were calculated, stratifying by type of stroke and HIV stage. Independent predictors of HIV infection were evaluated with multivariate logistic regression. Mortality, stay and cost per patient were also analyzed.

Results: From a total of 857.371 patients with stroke hospitalization, 2.226 had HIV infection. A 2.3% per year increase of the proportion of seropositive patients was observed, exclusively due to an increase of the ischemic strokes (per year-adjusted OR 1.033, CI 95% 1.018–1.046, $p < 0.0001$) and the asymptomatic stage of HIV infection (per year-adjusted OR 1.076, CI 95% 1.056–1.096, $p < 0.0001$). Factors independently associated with HIV infection were smoking, stimulating drugs consumption and HCV co-infection. HIV infection was associated with a higher mortality (OR 1.81, $p < 0.0001$), more days hospitalized (median: 11 vs 9 days, $p < 0.0001$) and a higher cost (median: 6.010€ vs 3.781€, $p < 0.0001$).

Conclusion: Over the last years, there is an increase in the proportion of HIV-infected patients, mainly asymptomatic, among stroke hospitalizations independently of other vascular risk factors. This finding suggests that HIV infection per se is a specific cerebrovascular risk factor.

Disclosure: Nothing to disclose

EP1102

Silent cerebral small vessel disease in cart well-controlled HIV-infected patients

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Background and aims: Cerebral small vessel disease (CSVD) is defined by white matter hyperintensities (WMHs), silent brain infarction (SBI) or microbleeds (MBs). cART well-controlled persons living with HIV (PLWHIV) are living longer and add conventional and non-conventional vascular risk factors (VRF), all that might act simultaneously to increase the prevalence of CSVD in PLWHIV.

Methods: The ANRS EP51 MICROBREAK (NCT02082574) cross-sectional study, aimed to assess the prevalence of CSVD in treated PLWHIV ≥ 50 years, with controlled viral load for at least 12 months; and to compare this prevalence to that observed in HIV negative controls (HNC). A logistic regression model was used to assess the impact of HIV on CSVD adjusted on traditional risk factors.

Results: 456 PLWHIV and 154 HNC were recruited; median age: 56 and 58 years ($p = 0.001$). All VRF were more frequent in PLWHIV than in HNC ($p < 0.004$), except diabetes. Median CD4 count was 655/mm³. CSVD was detected in 51.5% of PLWHIV and 36.4% of HNC, with an adjusted OR of 2.3 (95% confidence interval: 1.5–3.6). Older age and hypertension were associated with the risk of CSVD. The impact of HIV was different according to age, with ORa of 5.3, 3.7 and 1.0 for age of < 54 , 54–60 and > 60 years, respectively ($p = 0.022$). The proportion of participants with severe CSVD was 19% in PLWHIV and 14% in HNC, with an ORa of 1.6.

Conclusion: Prevalence of CSVD is twice higher in middle-aged PLWHIV. HIV is an independent risk factor of CSVD. Besides age and hypertension, HIV is an independent risk factor of CSVD.

Disclosure: grant from ANRS

EP1103

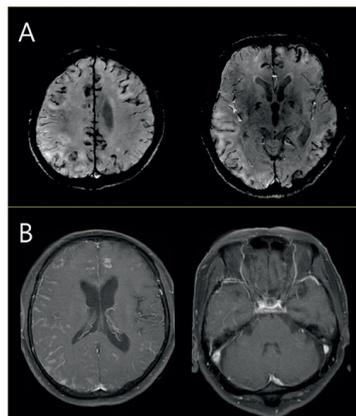
Respiratory virus-related meningoencephalitis in adults, South Korea, 2012-2015

C.-Y. Park, J.-S. Jun, S.-J. Ahn, T.-J. Kim, S.-T. Lee, K.-H. Jung, K.-I. Park, K. Chu, S.K. Lee
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Background and aims: The respiratory virus group consists of viruses such as adenovirus; respiratory syncytial virus (RSV) A and B; rhinovirus A and B; coronavirus, influenza A and B; parainfluenza 1, 2, 3; and metapneumovirus. RVs mainly cause upper or lower respiratory tract infections, but they can also cause central nervous system infection, mostly in children. Adult cases of RV-related meningoencephalitis have been reported in only a limited number of patients.

Methods: From March 2012 to December 2015, patients visiting Seoul National University Hospital with clinical suspicion of CNS infection were enrolled in the Seoul Neuroinfection registry. All patients underwent RV multiplex PCR analysis of the CSF and sputum.

Results: Among 661 patients, 10 patients were diagnosed with RV-related meningoencephalitis. Three patients showed positive CSF PCR results, including two with influenza A and one with human parainfluenza 3 virus. The other seven patients showed positive PCR results in the sputum. Six patients had preceding upper respiratory tract infection symptoms before manifestations of CNS infection. Leptomeningeal enhancement was the most frequent finding (70%) observed in MRI. Among the four RV-related encephalitis patients, three were treated with antiviral therapy. All patients completely recovered except one patient who deteriorated despite antiviral treatment



Brain MRI of an RV-related encephalitis patient with poor outcome (patient #3)

Conclusion: This is the first etiological study of adult RV-related meningoencephalitis in a large CNS infection registry. Clinicians should keep in mind that, although rare, RV can cause acute meningoencephalitis in adult patients. We suggest routinely screening for RV by multiplex PCR testing using CSF or sputum in adult encephalitis patients, even in those without URI symptoms.

Disclosure: Nothing to disclose

EP1104

Acute haemorrhagic leukoencephalitis after seasonal influenza vaccination

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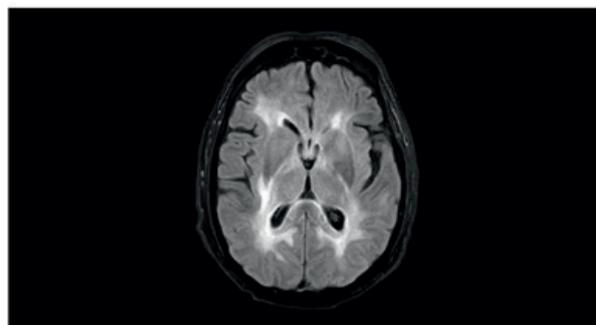
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Background and aims: To report a case of acute hemorrhagic leukoencephalitis (AHL) following influenza vaccination.

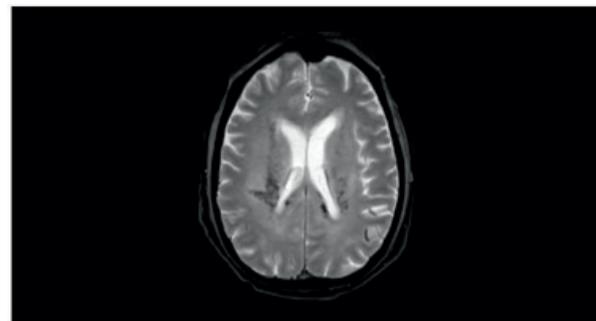
Methods: Case report

A previously healthy 70-year-old man presented with acute headache, fever, confusion, and left hemiparesis four days after influenza vaccination (Alpharix[®]).

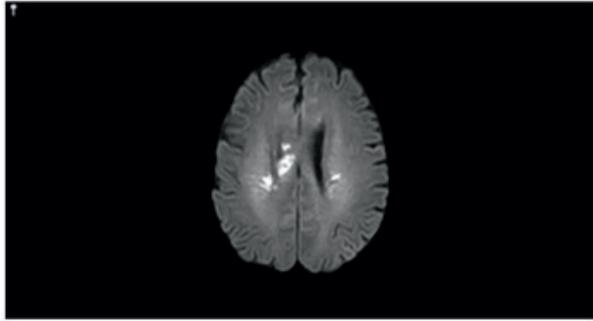
Results: Brain magnetic resonance imaging showed foci of microhemorrhage and extensive demyelinating lesions in the white matter, extending to the corpus callosum and the posterior part of the brainstem. Cerebral spinal fluid examination revealed a mixed leukocytosis with a high protein content. He was first given intravenous ceftriaxone, ampicilline, and acyclovir. Bacterial culture were negative as well as infectious and autoimmune serologies. Despite high dosis of corticosteroids and plasma exchanges, he developed a deep coma with spastic quadriplegia, decerebration signs, Cheyne-Stokes respiration, bilateral myosis, and absent oculo-cephalic reflexes. He died one month later.



MRI Flair



MRI Echogradient



MRI DWI

Conclusion: AHL is a variant of acute disseminated encephalomyelitis (ADEM), an inflammatory demyelinating disease of the central nervous system. The annual incidence of ADEM is estimated to 0.8/100.000. An history of previous vaccine is found in 5% of the cases, including both inactivated or virosomal influenza vaccinations. Our patient fulfilled the WHO causality assessment criteria for a probable diagnosis of AHL due to influenza vaccination. AHL can occur as a very rare complication of influenza vaccination and has a poor prognosis.

Disclosure: Nothing to disclose

EP1105

Central nervous system cryptococcosis in patients with different immunological status – clinical characteristics

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Background and aims: Central nervous system (CNS) cryptococcosis occurs in individuals with HIV or other immunosuppressions, such as autoimmune diseases, malignancies and post-transplantation, and immunocompetent patients. Our objective was to analyse clinical manifestations and prognosis in patients with different immunologic backgrounds, infected by *Cryptococcus neoformans* or *C. gattii*.

Methods: We performed a retrospective study of patients with CNS cryptococcosis treated in Hospital de Clínicas - Universidade Federal do Paraná, in southern Brazil, from 1987 to 2013. 247 patients were included and classified in 3 groups: (1) immunocompetent, (2) HIV+, or (3) immunodeficient HIV-. Data were compared using ANOVA and chi-square tests.

Results: 26 patients (10.5%) were immunocompetent, 200 (80.9%) were HIV+, and 21 (8.5%) were immunodeficient by another aetiology ($p < 0.0001$). Most were infected by *C. neoformans* ($n=233$, 94.7%), with a higher proportion among groups 2 ($n=197$, 98.5%) and 3 ($n=21$, 100%) than in group 1 ($n=15$, 57.7%), which had association with *C. gatti* infection ($p=0.008$). The commonest symptoms were headache ($n=195$, 78.9%), fever ($n=110$, 45.6%) and reduced consciousness ($n=67$, 27.8%). Group 1 had significantly higher age median (46.5 years) than groups 2 (35) and 3 (37), and higher rates of reduced consciousness ($n=13$, 50%, $p=0.04$), nuchal rigidity ($n=10$, 90.9%, $p=0.01$), ataxia ($n=6$, 24%, $p=0.006$) and paralysis ($n=12$, 48%, $p=0.007$). Mortality rates had no statistical differences between the groups. Neurologic sequelae were more frequent in group 1 ($n=7$, 28%, $p=0.0003$).

Conclusion: In CNS cryptococcosis, immunocompetence is associated with infection by *C. gattii*, higher age at onset, decreased level of consciousness, nuchal rigidity, motor symptoms, and sequelae.

Disclosure: Nothing to disclose

EP1106

Cancelled

Movement disorders 1

EP1107

Possibilities of gait training of Parkinson's disease treatment

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Background and aims: One of the most significant motor disorders in patients with Parkinson's disease (PD) is gait disorder. It is a decisive factor in determining the severity of the PD patients' condition and their quality of life. Usually, drug treatment not enough for gait disorders. Authors of abstract used self-development method of tempo-rhythmic correction (TRC) of gait (Russian Patent #2281695). The purpose of this study is evaluation effectiveness of TRC for gait correction.

Methods: Essence of TRC is special testing to select the individual frequency of auditory cues. During the gait synchronized with the tempo of the auditory stimulation. Gait trainee with step synchronization to an optimal frequency were held weekly, 3-6 times per day. We have two groups patient: control group (only drug treatment) (n=30) and experimental group (drug treatment plus TRC) (n=30). We assessment step parameters at baseline and 6 months later. We analyzed length of each step, average length of step and a special settlement parameter - the step of variability factor (SVF), which calculated under the formula: (the maximal length of step - the minimal length of step)/average length of step. SVF tend zero for healthy peoples. At Baseline both groups have 3 stage (Hoehn&Yarh) of PD, stable pharmacological treatment, without statistic significant differences.

Results: Results is presented at pic.1.

Time of Examination	Indicators	Group-1	Group-2
		Tempo-rhythmic correction	Control
Initial	Step-Variability-Factor (SVF)	0.51±0.09	0.52±0.06
	Average-Step-Length (ASL)	38.00±6.44	36.2±3.96
In 6 months	Step-Variability-Factor (SVF)	0.27±0.07*	0.40±0.06
	Average-Step-Length (ASL)	46.85±5.89*	38.21±3.73

*-p<0.05 (vs. control)

Conclusion: TRC method used in the treatment plans of PD patients, proved to be more effective in gait restoration compared to controls. Positive dynamics of the gait parameters (SVC, ASL) exceeded this PD patients whose treatment included only antiparkinson drugs.

Disclosure: Nothing to disclose

EP1108

The role of Clinical Outcome Assessment (COA) data in the drug approval process of medicines for the treatment of Restless Legs Syndrome (RLS): A review of the labels of medicines approved by the FDA and the EMA

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Background and aims: The objectives of this study were 1) to identify the medicines approved for the treatment of restless legs syndrome (RLS) by the Food and Drug Administration (FDA) and the European Medicines Agency (EMA); 2) to find out about the use of clinical outcome assessments (COAs) in the approval process; and 3) to identify the COAs endpoint positioning.

Methods: The EMA and FDA websites were explored to identify all medicines approved for RLS. The PROLabels database was used for labeling claim identification. All corresponding labels were reviewed for endpoint positioning.

Results: The agencies approved nine products with RLS indication (representing four INN, i.e., gabapentin, pramipexole, rotigotine, ropinirole); four products were approved by the FDA; five by the EMA, including one pramipexole generic. All products were evaluated using the same patient-reported outcome (PRO) measure, i.e., the International Restless Legs Syndrome Study Group Rating Scale (IRLS), which assesses disease severity. All had a similar claim, i.e., improvement in baseline IRLS score. The mean change from baseline in IRLS was a co-primary efficacy endpoint. The other COA used to develop a co-primary efficacy endpoint was a clinician-reported outcome (ClinRO) measure, either a Clinical Global Impression scale of Improvement (CGI-I) or a Clinical Global Impression scale of Illness Severity.

Conclusion: The patient's perspective is of paramount importance in the evaluation of medicines approved for RLS. The clinician input is also considered as a valuable endpoint since all evaluations were based on the use of co-primary PRO/ClinRO.

Disclosure: Nothing to disclose

EP1109

Translating the Rapid Eye Movement (REM) sleep behavior disorder screening questionnaire (RBDSQ) into 21 Languages using a standardized methodology

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Background and aims: The rapid eye movement (REM) sleep behavior disorder screening questionnaire (RBDSQ) is a 10-item patient self-rating scale, originally developed in German, using a Yes/No answer, which covers the clinical features of REM sleep behavior disorder. The objectives of this study were to present the method and the challenges of the RBDSQ translation into 21 languages.

Methods: In most languages, the translation process consisted of: 1) Conceptual analysis of the original RBDSQ with its developers; 2) Forward/backward translation step. The forward step (i.e., translation into the target language) used the German original and the UK English version as source versions to create two target versions, which were reconciled into one. This reconciled version was back-translated into English for quality check. For countries using a national variant of the same language (e.g., Australian English vs. UK English), an adaptation was performed.

Results: The translation process did not reveal any major difficulties since most of the behaviors assessed in the RBDSQ are cross-culturally relevant. Most of the issues belonged to the semantic and syntactic fields. For instance, the word “salutieren/saluting” created a range of queries (e.g., use formal vs. informal salute or both?) solved in collaboration with the developers. The translation of “Mücken verscheuchen/shooing away midges” led the translators to choose insects fitting their geographical location or colloquial expressions (e.g., “chasser les mouches” (flies) in French). Other examples are presented.

Conclusion: The multi-step rigorous translation methodology was key in developing 21 translations of the RBDSQ conceptually equivalent to the German original.

Disclosure: Nothing to disclose

EP1110

Cardiovascular autonomic dysfunction in parkinsonian disorders

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Background and aims: Autonomic disorders are the most frequent and severe symptoms of Parkinson's disease and atypical parkinsonism and a part of differential diagnostics.

Methods: Thirty-two patients were enrolled in the study (10 patients with Parkinson's disease (PD), 8 patients with Lewy body dementia (LBD); 8 patients with multiple system atrophy (MSA); 6 patients with progressive supranuclear palsy (PSP) - by clinical criteria). The control group - 10 healthy people without parkinsonism. The Valsalva maneuver was used to evaluate the cardio-vascular autonomic function via blood pressure changes and monitored by photometric method in beat-to-beat mode using NOVA Finapres, Netherlands.

Results: In the control group the systolic blood pressure (SBP) fall was 13.6 + - 2.1mmHg (p > 0.05); mean in 28 seconds. In PD patients 60.9 + - 7.4mmHg (p < 0.05), in 45 seconds. In PSP patients 56.0 + - 5.2mmHg (p < 0.05), in 25 seconds. In LBD patients 59.8 + - 8.1mmHg (p < 0.05), in 55 seconds. In MSA patients 99.2 + - 10.2mmHg (p < 0.05), in 30 seconds. Clinical manifestations of cardio-vascular autonomic dysfunction were identified in MSA and LBD patients.

Conclusion: The data showed a pathological type of autonomic response to Valsalva maneuver in patients with parkinsonian syndrome by comparison to control group. The pathological response characterized by the grade of the SBP fall and / or by the length of a cycle, with specific combinations of features for each type of parkinsonism. The clinical manifestations of cardiovascular instability were mainly associated with a length of blood pressure recovery.

Disclosure: Nothing to disclose

EP1111

Genotype may influence the onset of axial signs in early-stage Parkinson's disease

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Background and aims: Heterogeneity exists regarding the onset of axial signs in Parkinson's disease (PD). Dysarthria, swallowing disturbance and respiratory muscles dysfunction can be observed in early-onset PD patients. Due to their impact on the outcome and quality of life, evidencing risk factors of these symptoms is essential to optimize the follow-up of our patients. The aim of our study was to assess the association between the genotype and the axial signs.

Methods: MAPT haplotypes and COMT polymorphism were tested in 31 PD patients (mean age= 61.4 years±6.5) of the Prodigy-Park 1 cohort with a mean disease duration of 1.1 years (±1.1). Neurological, swallowing and voice and pulmonary function testing evaluations were performed.

Results: A valine homozygous polymorphism (n=11) was associated with a significantly higher sniff nasal inspiratory pressure (SNIP) in comparison with methionine homozygous (n=7) and heterozygous polymorphism (n=13) (78%±14.2 vs. 60.9%±19.8 - p=0.02). Regarding MAPT gene, patients with a H1/H1 haplotype (n=21) had a significantly higher severity of their dysarthria assessed by a French adaptation of the Frenchay Dysarthria Assessment (4±2.7 vs. 1.4±2.2 - p=0.02).

Conclusion: In early-stage PD, the onset of dysarthria or inspiratory muscle weakness might be associated with the genotype. Dopamine might impact on the ventilatory function and MAPT H1 haplotype could lead to a pseudobulbar palsy. These preliminary results need to be confirmed in a larger cohort to assess the influence of MAPT haplotypes or COMT polymorphism in the other features of the axial signs (such as the swallowing disturbance).

Disclosure: Nothing to disclose

EP1112

ParkLink Bologna - an Italian record linkage system for Parkinson's disease: Ready, set, go!

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M. Guarino⁹, F. Lucchi⁷, S. Nassetti², R. Pantieri¹⁰,
G. Samoggia⁷, T. Sacquegna¹¹, C.L. Scaglione²,
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Background and aims: Record linkage systems (RLS), matching data across administrative health databases, help providing information on diseased populations. However, detailed clinical information is often missing. The aim of the project (ParkLink Bologna) is to create a RLS based on clinical diagnosis to perform clinical epidemiologic studies on Parkinson's disease (PD) and parkinsonism (Ps) in a population-based setting (Bologna Health District, Emilia-Romagna Region, Italy).

Methods: Since January 2016, we are inviting neurologists working in private practice or public health service to enroll patients with a clinical suspect of PD or Ps residing in Bologna Health District (870507 inhabitants). Clinical diagnosis, date and type of onset and level of disability of patients who gave consent are linked to different administrative databases.

Results: On December 2016 six databases were linked (drug prescriptions, ER access, hospital discharges, copayment exemption, medical home-care, mortality); 15 neurologists out of 42 joined ParkLink. About 25% (539) of expected prevalent patients were already included (no refusals); 466 had a final diagnosis of PD (73%) or Ps (27%). Compared to Ps, PD were younger, with longer disease duration, lower disability level (Table 1) and a slightly different treatment prescribing pattern (Table 2). Risk of ER access and hospital admission increased with disability level.

Features	Parkinson's Disease N=339 N (%)	Parkinsonism N=127 N (%)	p-value
Age (years): mean (SD)	74.7 (8.7)	78.6 (7.6)	< 0.001
Gender:			0.110
M	215 (63.4)	70 (55.1)	
F	124 (36.6)	57 (44.9)	
Year of onset:			0.012
< 2008	100 (29.5)	22 (17.3)	
2008 – 2010	97 (28.6)	32 (25.2)	
2011 – 2013	96 (28.3)	47 (37.0)	
2014 – 2016	46 (13.6)	26 (20.5)	
Gelb's criteria:			
Possible	107 (31.6)		
Probable	232 (68.4)		
Hoehn and Yahr scale:			< 0.001
1	46 (13.6)	11 (8.7)	
1.5	43 (12.7)	5 (3.9)	
2	107 (31.6)	24 (18.9)	
2.5	47 (13.9)	17 (13.4)	
3	58 (17.1)	27 (21.3)	
4	31 (9.1)	31 (24.4)	
5	7 (2.0)	12 (9.4)	
Type of onset:			< 0.001
unilateral	281 (82.9)	46 (36.2)	
bilateral	58 (17.1)	81 (63.8)	
Type of onset_Tremor:			0.003
yes	223 (65.8)	62 (48.8)	
no	71 (20.9)	44 (34.7)	
missing	45 (13.3)	21 (16.5)	
Type of onset_Bradykinesia:			0.254
yes	233 (68.7)	95 (74.8)	
no	51 (15.1)	19 (15.0)	
missing	55 (16.2)	13 (10.2)	
Follow-up (months): mean (SD)	5.1 (3.7)	5.0 (3.7)	0.664

Table 1. Distribution of demographic and clinical features of patients with diagnosis of Parkinson's Disease and parkinsonism.

Treatment	Parkinson's disease N= 339 N (%)	Parkinsonism N= 127 N (%)	p-value
Levodopa only	105 (31.0)	68 (53.5)	< 0.001
Levodopa + Dopamine Agonists	135 (39.8)	23 (18.1)	< 0.001
Levodopa + MAO B Inhibitors	14 (4.1)	9 (7.1)	0.23
Levodopa + Dopamine Agonists + MAO B Inhibitors	31 (9.1)	3 (2.4)	< 0.001
Dopamine Agonists only	19 (5.6)	7 (5.5)	1.00
MAO B Inhibitors only	4 (1.2)	0 (0.0)	0.58
Dopamine Agonists + MAO B Inhibitors	6 (1.8)	2 (1.6)	1.00
No Levodopa, Dopamine Agonists or MAO B Inhibitors	25 (7.4)	15 (11.8)	0.14

Table 2. Distribution of prescribing treatments in patients with Parkinson's Disease and parkinsonism.

Conclusion: ParkLink is an independent, publicly funded RLS based on clinical diagnosis linked to administrative databases. Neurologists' recruitment is ongoing and a website is published (www.isnb.it/ricerca/parklink). Preliminary findings show that such a system may produce relevant data on clinical epidemiology and burden of disease concerning PD and Ps.

Disclosure: Nothing to disclose

EP1113

Cancelled

EP1114

Persistent L-Dopa responsive hemiparkinsonism after cryptococcal meningoencephalitis in an immunocompetent man

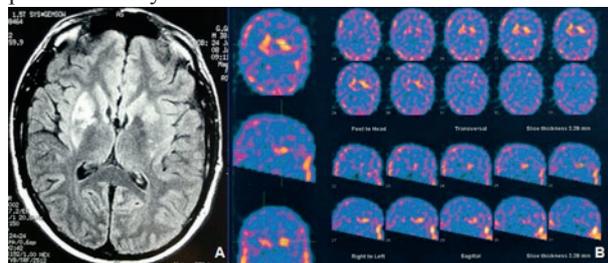
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Background and aims: Secondary parkinsonism due to infectious disorders might present with either generalized or more lateralized symptoms with an acute/subacute evolution. However, documented basal ganglia dopamine depletion in the setting of infectious meningoencephalitis is quite rare. We aim to report the case of an immunocompetent male who had hemiparkinsonism responsive to L-Dopa therapy following cryptococcal meningoencephalitis.

Methods: Case report.

Results: A 43-year-old Caucasian immunocompetent male was admitted to the hospital with a proved diagnosis of meningoencephalitis, with fever, severe headache, mental confusion and somnolence. CSF analysis disclosed *Cryptococcus neoformans*. Brain MRI showed images on right basal ganglia compatible with Cryptococcal abscesses, which later evolved to encephalomalacia on the right striatum on a follow-up exam after adequate treatment with amphotericin B and ventricular shunt (Figure 1 - a). At the time of hospital discharge from the hospital he had developed with left hemiparkinsonism and mild cognitive decline. A brain SPECT with TRODAT-1 (Figure 1 -b) demonstrated moderate reduction of dopamine transporter binding on the right striatum. The patient was treated with levodopa-benserazide 100/25mg thrice daily, with remarkable improvement of the parkinsonian syndrome.



Brain T-1 weighted MRI showing right basal ganglia encephalomalacia secondary to the Cryptococcal abscesses (A). Brain SPECT with TRODAT-1 shows moderate reduction of DTA binding on the right striatum and normal binding on the opposite side (B).

Conclusion: Hemiparkinsonism secondary to Cryptococcal meningoencephalitis leading to striatum encephalomalacia is a rare etiology of secondary parkinsonism, even more so with documented dopamine depletion.

Disclosure: Nothing to disclose

EP1115

Acute restless legs syndrome after liposuction surgery, with hypoxic-ischemic encephalopathy, associated with Pramipexole-induced kleptomania

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Background and aims: Recently functional neuroimaging studies have suggested that RLS can result from dysfunction of the dopaminergic system in the striatum. Our goal is to report a case of acute RLS following liposuction with hypoxic-ischemic encephalopathy, associated with kleptomania induced by the therapeutical use of pramipexole.

Methods: Case report.

Results: A 40-year-old woman who had previously undergone bariatric surgery underwent liposuction for aesthetic purposes. In the post-operative period of liposuction she presented with somnolence, mental confusion, temporal-spatial disorientation and working memory deficits, later followed by severe and unpleasant discomfort in her lower limbs, which was characterized by pain and severe spasms at rest, particularly at night, with improvement of these symptoms while walking. Brain MRI demonstrated scattered and diffuse nearly symmetrical lesions in the BG and cerebellum suggestive of hypoxic-ischemic insults. A subsequent MRI suggested that most lesions vanished leaving cystic cavitations on the lenticular nucleus and caudate and brain -tractography analysis showed a reduction in fractional anisotropy. Thus, she was diagnosed with acute RLS, following acute hypoxic-ischemic encephalopathy after liposuction, and started on pramipexole 0.5mg qid at bedtime. RLS symptoms subsided with normalization of her sleep pattern. However, after 3 months of pramipexole treatment she developed symptoms of kleptomania. Pramipexole was titrated to a lower dose (0.125mg) with resolution of kleptomaniac symptoms.

Conclusion: The behavioral changes observed in our patient, including kleptomania, most likely arose from failure of inhibitory pathways involving basal ganglia, prefrontal cortex and limbic structures, and was triggered by the pramipexole treatment, suggesting an impulse control disorder.

Disclosure: Nothing to disclose

EP1116

Tetrabenazine versus deutetabenazine for Huntington's disease: Twins or distant cousins?

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Background and aims: Tetrabenazine is the only FDA-approved drug for Huntington's disease (HD), and deutetabenazine was recently tested against placebo. A switching-trial from tetrabenazine to deutetabenazine is underway, but no head-to-head blinded, randomized controlled trial (RCT) is planned. Using meta-research methodology, we compared these molecules.

Methods: RCTs comparing tetrabenazine or deutetabenazine with placebo in HD were searched. We assessed the Cochrane risk of bias tool, calculated indirect treatment comparisons, and applied the GRADE approach.

Results: Our evidence network comprised one tetrabenazine and one deutetabenazine trial, both against placebo. Risk of bias was moderate in both. Tetrabenazine and deutetabenazine did not differ significantly on motor scores or adverse events. Depression and somnolence scales favoured deutetabenazine significantly.

Conclusion: There is low-quality evidence that tetrabenazine and deutetabenazine do not differ in efficacy and safety. Importantly these results are likely to remain the only head-to-head comparison between these compounds in HD.

Disclosure: Nothing to disclose

EP1117

An observational study of the motor and non-motor effects of deep brain stimulation, intrajejunal levodopa infusion, and oral levodopa in advanced Parkinson's disease

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Background and aims: Subthalamic nucleus deep brain stimulation (STN-DBS), continuous infusion of levodopa/carbidopa gel and oral levodopa are effective treatment for both motor and nonmotor symptoms (NMS) of Parkinson's disease (PD). However, the available studies have focused mainly on the effects of STN-DBS and infusion therapies, there are few specific comparative studies.

Methods: In this randomized study, we compared the effect of oral levodopa treated versus intrajejunal levodopa versus subthalamic nucleus deep brain stimulation (STN-DBS) on the different characteristics of NMS in patients with advanced PD.

Results: One hundred and fourteen Parkinson's patients satisfying the UK PD Brain Bank criteria for diagnosis of idiopathic PD participated and assessed using NMS questionnaire (NMSQuest), UPDRS, Hoehn and Yahr classification, Hospital Anxiety Depression Rating Scale (HADS). The results of NMSQ for all three groups were found equal.

Subdomains	Deep brain stimulation	Dopamin agonists or levodopa	Duodopa infusion	*p
	Median (Q1, Q3)	Median (Q1, Q3)	Median (Q1, Q3)	
Urinary tract	2 (1, 2)	2 (1, 2)	2 (1.5, 2)	0.422
Sexual function	2 (0, 2)	2 (0, 2)	1.5 (0.5, 2)	0.641
Sleep	2 (1, 3)	2 (1, 3)	3.5 (2.5, 4)	0.638
Depression/Anxiety	2 (0, 2)	1 (0, 2)	1 (0.5, 1.5)	0.626
Total	14 (10, 16)	13 (9, 17)	15.5 (14.5, 16.5)	0.818

Table : Correlation between three groups.

Conclusion: Several studies have shown that levodopa-based dopaminergic stimulation is beneficial for NMS and health-related quality of life in PD in addition to the reduction of motor fluctuations and dyskinesias.

Disclosure: Nothing to disclose

EP1118

Late-onset levodopa responsive parkinsonism due to POLG mutations

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Background and aims: Polymerase gama (POLG) mutations have been described in association with wide a spectrum of phenotypes. Parkinsonism is unfrequently described and usually a late feature in patients with progressive external ophthalmoplegia.

Methods: Case report.

Results: We describe a 76-year-old gentleman with REM-sleep behavior disorder (RBD) since the age of 61, who developed shuffling gait and stooped posture by 63-year-old, and a year later left-hand resting tremor. Personal/family history were unremarkable. When observed, age 64, he presented hypomimia, left-predominant parkinsonism, camptocormia, short-step shuffling gait and postural instability. He had frontal bossing conferring him a peculiar face, and oversized hands. Levodopa/carbidopa was started with moderate improvement. Brain MRI revealed widespread partially confluent cerebral white matter lesions. An extensive blood/CSF workup was conducted with normal/negative results. Muscle biopsy showed rare ragged-red and COX-negative fibers. EMG excluded myopathy/polyneuropathy. Mitochondrial chain complex activity was normal; however multiple mitochondrial DNA deletions were identified. POLG gene study revealed deletion c.127_132delCAGCAG and point mutation p.G268A(c.803G>C), in compound heterozygosity, already described as pathogenic. Cognitive decline began by 65, and a year later motor fluctuations appeared. Over 12 years there was moderate progression. He now presents cognitive impairment, fragmented pursuit ocular movements (without ophthalmoplegia) and levodopa responsive parkinsonism(video).

Conclusion: The reported patient presents a rare phenotype of POLG mutations: late-onset levodopa-responsive asymmetric parkinsonism, with RBD and motor fluctuations, in the absence of progressive ophthalmoplegia and neuropathy. It was the presence of early gait impairment and postural instability associated with subtle facial dysmorphism, which prompted additional investigation leading to the final diagnosis.

Disclosure: Nothing to disclose

EP1119

Cognitive impairment as FXTAS debut

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Background and aims: Fragile X-associated tremor/ataxia syndrome (FXTAS) is a neurodegenerative disorder caused by a premutation in the fragile X mental retardation 1 (FMR1) gene, including as the major clinical criteria tremor and cerebellar ataxia. Retrospective reports show that over 50% of patients have cognitive changes. In fact, those with T2 white matter hyperintensities in the middle cerebellar peduncles (MCP sign)– cardinal radiological sign– are likely to have more severe cognitive deficits.

Methods: We present a 59-year-old man with memory and executive impairment, without previous intellectual disability nor family history, and normal physical examination. In the following 2 years he suffered progressive cognitive deterioration with functional disturbance. In addition, partial seizures, tremor and cerebellar ataxia arose.

Results: Based on the clinical evolution, cranial MRI was reviewed, evidencing the MCP sign, and genetic molecular test for FMR1 gene was performed, confirming the expansion in premutation range. Considering all results, the definitive diagnosis of FXTAS was established.

Conclusion: FXTAS prevalence is estimated about 1 in 3,000 men. Nevertheless, FXTAS is under-recognized and frequently misdiagnosed. Our case is atypical as cognitive impairment without additional features is a rare cause of initial consultation and dementia remained as the predominant feature in early stages. We suggest that this genetic test should be at least considered in cases of unexplained cognitive decline, especially if characteristic white matter lesions on MRI are seen. This case additionally supports that the original diagnostic criteria need to be updated, in order to improve the identification of affected persons due to the expanding phenotypes that are nowadays known.

Disclosure: Nothing to disclose

Movement disorders 2

EP1120

Dopamine transporter imaging and cardiac MIBG in patients with parkinsonism: A case for heterogeneity

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Background: Severe DatScan deficiency is usually correlated with severe motor deficit. Furthermore Parkinson's disease (PD) is characterized by a variety of NMS of which some might be associated with cardiac sympathetic denervation.

Aims: To explore cardiac sympathetic function and clinical non-motor symptoms (NMS) expression in patients with severe DatScan depletion. The relation between the two is unclear.

Methods: Patients who underwent a cardiac MIBG scan, DatScan imaging and completed clinical assessment including the NMSScale were retrospectively reviewed in this going on study. DatScan and cardiac MIBG uptake were classified as normal (>2), or mild ($1.5 > < 2$), moderate ($>1, < 1.5$) and severe (< 1) reduction. The NMSburden (NMSB) was assigned according to the NMSScale in mild, moderate, severe and very severe (Chaudhuri et al., 2006).

Results: All nine patients presenting with Parkinsonism had severe dopaminergic depletion in the putamen with an uptake ratio < 1.0 (mean putamen uptake right 0.6 ± 0.2 and left 0.8 ± 0.3). Three patients showed a moderately reduced uptake on cardiac MIBG (R1 ratio < 1.5), five patients showed a mild reduction (R1 ratio < 2) and one patient showed normal cardiac uptake (R1 ratio > 2). One patient reported mild NMSB, one reported moderate NMSB, three reported severe NMSB and four reported very severe NMSB.

Conclusion: In spite of the severe putaminal dopaminergic depletion, the patients expressed a very heterogeneous presentation of cardiac MIBG scan and NMSB even in this small sample. This highlights the fact that possibly also PD is rather a complex syndromic condition than a disease.

Disclosure: Nothing to disclose

EP1121

Long-term effects of safinamide treatment on pain in fluctuating Parkinson's disease patients

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Background and aims: Safinamide (Xadago[®], Zambon SpA Italy), is a new drug with a dual mechanism of action (dopaminergic and non-dopaminergic). Results of the pivotal trials showed an increase in "ON" time and a decrease in "OFF" time maintained up to two years. This post-hoc analysis investigates the long-term efficacy of safinamide vs placebo on pain in parkinsonian patients with motor fluctuations.

Methods: The effects of safinamide on the reduction of concomitant pain treatments and on the items related to pain of the Parkinson's disease Quality of life questionnaire PDQ-39 were investigated using the data from the pivotal Phase III trial 018.

Results: The percentage of patients with no pain treatments at the end of two years were significantly lower in the safinamide group compared to the placebo group (61.1 vs 50.9%; $p=0.0478$), with an average reduction of the individual use of pain treatments by 26.2%. Moreover, safinamide significantly improved the PDQ-39 pain-related items.

Conclusion: Safinamide, administered as add-on therapy in fluctuating parkinsonian patient, significantly reduced the number of concomitant pain treatments, maintaining the efficacy up to two years. These results suggest that safinamide may have a positive effect on pain, one of the most underestimated non-motor symptoms of parkinsonism.

Disclosure: Carlo Cattaneo and Ioannis Kottakis are Zambon SpA employees. Erminio Bonizzoni is Zambon SpA consultant

EP1122

Cancelled

EP1123

Autonomic testing in patients with Parkinson-plus syndromes

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Background and aims: Corticobasal degeneration (CBD), multiple system atrophy (MSA) and progressive supranuclear palsy (PSP) consist the Parkinson-plus syndromes. Despite distinct clinical features, differential diagnosis is problematic, particularly in atypical cases or in the early stages of these disorders. The objective of this study was to examine the usefulness of bedside autonomic testing in the differential diagnosis of Parkinson-plus patients.

Methods: A total of 51 Parkinson-plus patients were included (17 CBD, 15 MSA and 19 PSP). Autonomic testing included the heart rate response to breathing (R-R test) and the presence of orthostatic hypotension (reduction of systolic (SBP) and diastolic blood pressure (DBP) within 1 and 3 minutes of standing from the supine position). Analysis of variance, Kruskal-Wallis and ROC curve analysis tests were used as appropriate.

Results: MSA patients differed significantly from the other two groups in the SBP and DBP drop from 0 to 3min and from 0 to 1min when standing from the supine position. There was no difference in the heart rate variability during standing or in the R-R test. SBP difference from 0 to 3min was most potent in discriminating MSA patients (AUC=0.89, $p<0.0001$, sensitivity 80%, specificity 85.2% for a cut-off point of $>20\text{cm H}_2\text{O}$ BP drop).

Conclusion: SBP drop of $>20\text{cm H}_2\text{O}$ cut-off during standing from a supine position (compared to the more stringent $>30\text{cm H}_2\text{O}$ of the diagnostic criteria) can discriminate MSA patients from other Parkinson-plus patients, with adequate sensitivity and specificity. The R-R test does not differentiate among Parkinson-plus patients.

Disclosure: Nothing to disclose

EP1124

How do Parkinson's disease patients manage Ramadan fasting?

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Background and aims: Although Ramadan fasting is not mandatory for patients suffering from chronic disease, many patients are tied to respect it. To our knowledge, no previous studies have analyzed how PD patients manage Ramadan fasting.

Methods: Twenty four PD patients (60.4 years, 9 females) seen in the outpatients department of Ibn Sina Hospital (Kuwait city) having planned to fast during the 2016 Ramadan were included. They underwent a clinical interview and a neurological examination, including the (MDS-UPDRS), the Hoehn and Yahr staging scale, the (NMS), the (PDQ-39) and the clinical impression of severity index for Parkinson disease (CISI-PD). Assessments were performed 2 to 4 weeks before Ramadan and 2 to 4 weeks after, 20 patients fulfill the whole fasting period.

Results: Mean disease duration was 5.8y with a Hoehn and Yahr score at 1.8. Fourteen patients were treated with a combination of L-DOPA and DA, one patient with DA monotherapy and five patients were treated with L-DOPA monotherapy with a (LEDD) of 820mg (150-1584); 3 patients were treated with subthalamic DBS. 6 patients were able to have no drug intakes between dusk and dawn; others patients needed to take 1 or 2 intake of L-DOPA inbetween. Eight patients maintained the same LEDD, 10 decreased it, and 2 increased it. No serious side effects were reported, there were no significant changes after the fasting period in PDQ 39, NMS, CISI.

Conclusion: With some adjustments in the treatment, patients with mild to moderate PD appear to manage Ramadan fasting well without serious damage to their health.

Disclosure: Nothing to disclose

EP1125

Colic fistulisation of jejunal tube in a Parkinson's disease patient under Duodopa® therapy

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Background and aims: In patients with advanced Parkinson's disease (PD), the continuous delivery of levodopa/carbidopa gel (Duodopa) through a percutaneous endoscopic gastrostomy with jejunal extension (PEG-J) allows less variability in levodopa concentrations and results in fewer motor complications compared with oral administration. Over the past years, some severe gastrointestinal complications have been described in patients with Duodopa®.

Methods: We report a serious gastrointestinal complication associated with Duodopa® therapy.

Results: A 53-year-old woman with PD began Duodopa® therapy through a PEG-J due to motor complications, with excellent response to treatment. Three years later she reported loss of Duodopa® efficacy and worsening of Parkinson symptoms, warranting oral levodopa medication with symptom improvement. A gastroscopy revealed gastrostomy tube erosion through the duodenum wall. Contrast-enhanced computer tomography of the abdomen revealed migration of the jejunal tube through multiple downstream entero-enteric fistula with the distal end situated in the ascending colon. Colonoscopy revealed tube tip entrapment by phybezoar with resistance to mechanical pull by endoscopic snare. Removal of the PEG was performed with proximal cut of the jejunal tube, and 2 days later complete anal exteriorization of the remaining tube spontaneously occurred without any complications.

Conclusion: This case illustrates that loss of response to Duodopa® therapy should alert the clinician to some potentially severe complications and should grant prompt endoscopic examination. Unlike some fatal cases published in the literature, our patient spontaneously expelled the jejunal tube without any complication. We believe that in particular cases an expectant attitude should be considered as an option.

Disclosure: Nothing to disclose

EP1126

Isolated dystonia caused by ATP1A3 mutation unresponsive to deep brain stimulation

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Background and aims: Mutations in the ATP1A3 gene are associated with a wide spectrum of neurologic disorders encompassing rapid-onset dystonia-parkinsonism (RDP) and alternating hemiplegia of childhood (AHC). Isolated dystonia has been occasionally reported. The efficacy of deep brain stimulation (DBS) in cases of isolated dystonia with ATP1A3 gene mutations has not been established.

Methods: We reported the outcome, after ten years of stimulation adjustments, in a patient with ATP1A3 isolated dystonia who received a GPi DBS implant and then compared the results to all published cases of ATP1A3.

Results: Our patient bore a heterozygous de novo missense mutation (c.1250T>C, p.L417P) in the ATP1A3 gene, had isolated dystonia and did not respond to GPi DBS. Overall, seven cases with isolated dystonia were reported and four ATP1A3 dystonic patients have received stereotactic surgery in the GPi; no patient has received surgery in other targets. The mutation found in this case of isolated dystonia has been previously observed in one patient with RDP.

Conclusion: We report failure of GPi stereotactic surgery in five patients with ATP1A3, including this observation with isolated dystonia and one case of pallidotomy without mention of parkinsonism. We also confirm clinical and genetic heterogeneity of this condition. ATP1A3 dystonia may possibly represent a case of "surgicogenomics", meaning that such genetic diagnosis may be a negative indication for stereotactic surgery in the GPi. It remains unknown whether DBS in other targets may be efficacious.

Disclosure: Nothing to disclose

EP1127

Monotherapy with perampanel as an alternative for refractory myoclonusE.D. Diaz Pertuz¹, J. Pagonabarraga², J. Kulisevsky³¹Pamplona, Spain, ²Neurología, Hospital de la Santa Creu i Sant Pau, España, Spain, ³Barcelona, Spain

Background and aims: Myoclonus is a sudden, brief, shock-like, involuntary movement. Cortical myoclonus treat is often refractory and requires the use of polytherapy being the dose occasionally limited by the onset of side effects. The aim of this study is to report three patients with drug-resistant chronic myoclonus that had not improved with clonazepam, levetiracetam and valproic acid, but improved markedly after onset with perampanel.

Methods: Three case reports. Patients unresponsive for available drugs for myoclonus were started on perampanel in monotherapy. Patients were video-taped before and after achieving therapeutic full dose with perampanel, and change on myoclonus severity was assessed by the Clinical Global Impression of Change (CGI-C) scale.

Results: Two adult patients with myoclonus as a sequelae of hypoxic-ischemic brain injury during the perinatal period, and one young woman with drug-induced myoclonus started treatment with perampanel after conventional polytherapy for chronic myoclonus. Global improvement was rated as “much improved” in two patients (CGI-C=2), and “very much improved” in one patient (CGI-C=1). Global improvement was associated with an improvement in daily functionality and recovery of tasks that have been withdrawn because of myoclonus. Two patients experienced improvement at 4mg/day, and one at 6mg/day. During titration phase, three patients experienced dizziness 10-15 minutes after taking the drug, but good tolerance was achieved after 1 month of treatment.

Conclusion: Perampanel appears as a good alternative in patients with drug-resistant myoclonus. Based on these anecdotal cases, clinical trials seem promising for further assessing the efficacy of perampanel for refractory chronic myoclonus.

Disclosure: Nothing to disclose

EP1128

Cancelled

EP1129

Psychiatric disorders and personality traits in patients with essential tremorN. Dragasevic Miskovic¹, A. Tomic¹, N. Kresojevic¹, D. Pesic², A. Potrebic³, M. Kostic², I. Petrović¹, S.Z. Peric¹, V. Kostic¹¹Movement Disorders Department, Clinic for Neurology, Clinical Centre of Serbia, Belgrade, Serbia, Faculty of Medicine, University of Belgrade, Belgrade, Serbia,²Institute of Mental Health, Faculty of Medicine, University of Belgrade, Belgrade, Serbia, ³Clinic for Psychiatry, Clinical Centre of Serbia, Belgrade, Serbia

Background and aims: Essential tremor (ET) can have more complex motor features (e.g. ataxia), likewise different non-motor manifestations regarding both cognitive and psychiatric symptoms. The aim of the work was to determine psychiatric disorders and personality pattern in a cohort of ET patients, and to assess relation between motor and non-motor features of ET.

Methods: ET patients (101) were examined for the presence of psychiatric disorders according to DSM IV criteria. All patients were evaluated by standardized psychiatric and neurologic battery of tests. Personality profile was assessed by Millon Clinical Multiaxial Inventory III (MCMI).

Results: ET patients (age 49.6±18.6, disease duration 15.6±14.4) were divided in two groups, early onset ET (EOET) and late-onset ET (LOET). Depression (according to SCID-I), and obsessive-compulsive personality disorder (SCID-II) were the most prominent psychiatric disorders in both groups. MCMI scores above 75, indicating presence of specific personality trait, were found for paranoid personality trait, and for psychotic depression among psychiatric symptoms. Associations between dominant personality characteristics and main clinical and demographic factors showed that narcissism and anxiety were in correlation with ADL (p=0.039, p=0.007) and social burden (p=0.014, p=0.001), whereas major depression was in correlation with social handicap (p=0.002), severity of tremor (p=0.019), ADL (p=0.006), and social burden (p=0.049).

Conclusion: Our research confirms that ET is more than a disease of motor system. A significant number of patients suffer from psychiatric disorders, with a high frequency of specific personality disorders.

Disclosure: Nothing to disclose

EP1130

The spatiotemporal gait parameters assessment in Wilson's disease patients

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Background and aims: Wilson's disease (WD) is an inherited disorder of copper metabolism. Gait disturbances may present with both extrapyramidal and cerebellar patterns. Our previous study showed that gait abnormalities are observed in almost 60% of WD patients. The most frequent was ataxic gait (45%) characterized mainly by impaired tandem. So far spatiotemporal gait parameters were not established in WD patients. The aim of our study was to characterise basic objective gait parameters.

Methods: We analysed gait parameters in 34 WD patients in comparison with 28 healthy controls. Spatiotemporal parameters: velocity, cycle time, cadence, base of support was assessed using GAITRite walkway system. Clinical neurological assessment was based on Unified Wilson's Disease Score Scale (UWDRS).

Results: We examined 16 neurologic and 18 hepatic WD patients, and compared their results with healthy control group. Velocity of gait was lower in neurologic group ($p=0.03$), and not differ from control group in hepatic subjects ($p=0.15$). Cadence was decreased in neurologic patients ($p<0.0001$) as well as in hepatic ($p<0.005$). Neurologic group had had statistically significant wider base of support ($p=0.002$) as compare to control group.

Conclusion: Our study shows in objective analysis, gait disturbances in WD neurologic patients compared to healthy controls. Notably, subjects with WD demonstrated wider base of support than control group. This is in accordance with our previous clinical observation that impaired tandem gait is common. Although neurologic WD patients presented markedly impaired gait, in hepatic patients we observed decreased cadence. Further analysis on larger group of WD patients is needed to provide insight into gait disturbances.

Disclosure: Nothing to disclose

EP1131

Effects of Chronic Pain on Quality of Life, Depression, Anxiety, Fatigue and Sleep Quality in Turkish Patients with Parkinson's Disease

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Background and aims: There are limited researches in literature evaluating the exact relationships between pain, and other comorbid symptoms like mood and sleep in patients with Parkinson's disease (PD). In this study, we aimed to explore the characteristics of chronic pain and its effects on quality of life, anxiety, depression, fatigue, and sleep quality.

Methods: Forty one patients with PD and 21 healthy controls matched for age and gender were included. The Unified PD Rating Scale and Hoehn&Yahr stage were used to assess motor disability and disease severity. Patients examined relating to the characteristics of the chronic pain. All subjects completed Beck Depression and Anxiety Inventories, Parkinson's Disease Questionnaire, Pittsburgh Sleep Quality Assessment, Fatigue Severity Scale questionnaires.

Results: Twenty eight patients (68%) suffered from chronic pain. Of these, 48% had musculoskeletal, 14% radicular/peripheral neuropathic, 9% dystonia related, 4% central parkinsonian, 14% headache, and 2% vascular pain respectively. Nine patients (21%) had two or more types of pain. Comparing PD patients with and without pain and their demographical and clinical features and mean quality of life scores, there were not any statistical differences. We found that mean depression, anxiety and sleep quality scores between PD patients with and without pain and control group were not stastically significant. Furthermore, there was not correlation between pain and depression, anxiety, fatigue and sleep quality.

Conclusion: There are different pain types co-existing in patients with PD. Despite the previous studies, our findings support that pain does not affect patients' quality of lives and other non-motor symptoms such as depression, anxiety, fatigue and sleep.

Disclosure: Nothing to disclose

EP1132

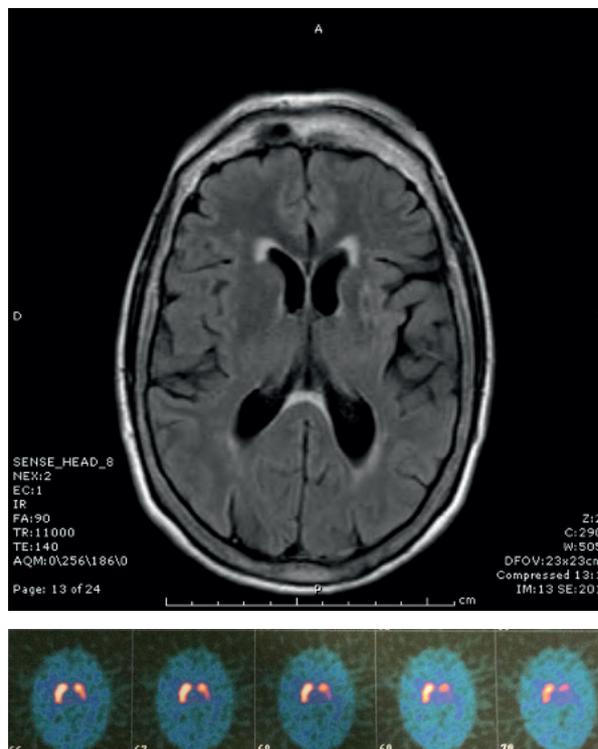
Subacute hemichorea associating dopamine depletion in basal ganglia and cerebral hemiatrophy

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Background and aims: There are few etiologies of subacute hemichorea. Common causes structural lesions or nonketotic hyperglycemia. The association with contralateral dopamine depletion or cerebral atrophy is uncertain.

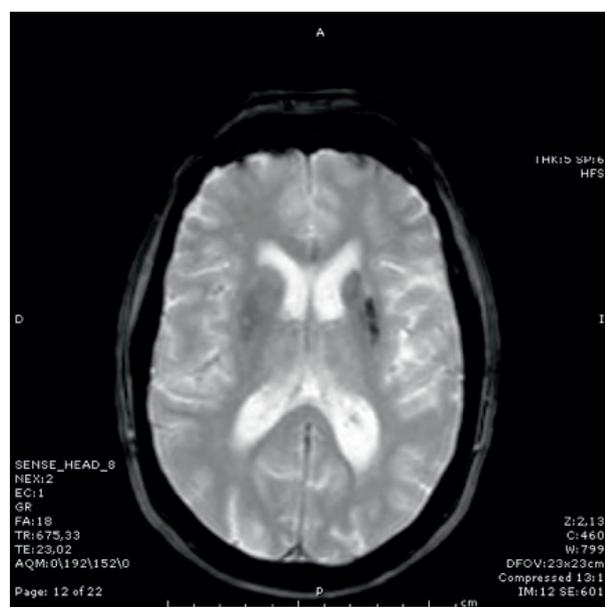
Methods: Case report

Results: We present a woman aged 57 whose past history included dyslipidemia, diabetes mellitus and depression treated with clonacepam and venlafaxine. She presented to our clinics due to involuntary movements involving right hemibody that appeared gradually over the past 3 months. Neurologic examination disclosed choreic movements affecting right extremities. Movements increased with distraction and disappeared while sleeping. There were neither parkinsonian signs nor limb atrophy. Supraaortic trunk sonography was also normal. Complete blood and cerebrospinal fluid analysis including biochemistry, glucose, immunology and, microbiology were all normal. Genetic analysis of Huntington's disease was negative. MRI showed atrophy of left cerebral hemisphere (figures 1,2). DaTscan (figure 3) was performed disclosing marked reduction of presynaptic nigrostriatal dopamine affecting left caudate and putamen. 10 years after disease onset the patient still has choreic movements affecting right hemibody.



Conclusion: We present a patient with right hemichorea with left basal ganglia dopamine depletion and left hemicerebral atrophy of unknown significance.

Disclosure: Nothing to disclose



MS and related disorders 1

EP1133

Correlation between retinal nerve fiber layer thickness and presence of IgM oligoclonal bands in relapsing-remitting multiple sclerosis

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Background and aims: Axonal degeneration is related to the development of neurologic disability in multiple sclerosis (MS). We studied the correlation between the presence of IgM oligoclonal bands (OB) in the CSF, a biological marker of poor prognosis, and the degree of axonal degeneration as measured by the thinning of retinal nerve fiber layer (RNFL).

Methods: Fifty-one consecutive patients with a recent diagnosis of RRMS were included (≤ 5 years since first attack) and divided into two groups according to the presence/absence of IgM OB. Sociodemographic and clinical variables were collected and optical coherence tomography (OCT) was performed.

Results: Mean age was 37.14 years, 62.75% were women. Median time from first attack to recruitment was 2.18 years (range 0.35–3.89). One-hundred and two OCT explorations were performed, 52 of them belonging to the IgM OB group. In this group, we found a statistically significant reduction of RNFL thickness on the temporal quadrant ($59.30\mu\text{m}$, SD 13.19) as compared to the group without IgM OB ($64.49\mu\text{m}$, SD 11.81), $p=0.03$.

The examination of those eyes without history of optic neuritis ($n=89$) showed a thinner temporal quadrant of CFNR in the group with IgM OB ($61.88\mu\text{m}$, SD 11.81) as compared to the group lacking IgM OB ($65.07\mu\text{m}$, SD 10.80), without reaching statistical significance ($p=0.23$).

Conclusion: Patients with IgM OB present a thinner CFNR on the temporal quadrant from early stages. This tendency must be confirmed on follow-up studies (ongoing).

Disclosure: This research has been funded by the Health Department of the Basque Government

EP1134

The expression of matrix metalloproteinase peripheral profile in multiple sclerosis patients treated with natalizumab: Possible additional mechanisms of natalizumab action

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Background and aims: Natalizumab (NAT) is a powerful treatment in multiple sclerosis (MS) patients that was designed with a clear mechanism of action (inhibition of $\alpha 4$ -integrin, the key molecule of brain homing). Still, approximately a third of treated patients continue to present disease activity due to blood-brain barrier (BBB) damage. In MS, Matrix Metalloproteinases (MMPs) are involved in BBB dysfunction, leading to the perpetuation of neuroinflammation.

Objectives: Evaluation of the evolution of a panel of MMPs during NAT treatment in MS patients.

Methods: 30 RRMS patients (mean MS duration 10.5 years) treated with NAT (mean duration 21.7 months) and 30 healthy subjects were tested using a Bio-PlexPro™ Human MMP Panel (MMP-1, MMP-2, MMP-3, MMP-7, MMP-8, MMP-9, MMP-10, MMP-12, MMP-13) through Multiplex method. The study had a mean duration of 9 months and the patients underwent clinical, MMP and brain MRI evaluation at the inclusion and at the end of the research. Statistical analysis considered significant values: $p \leq 0.05$.

Results: NAT decreased the peripheral values of MMPs (in MMP-9 and MMP-3 statistical significance was found). In patients that had relapses before and during the study, values of MMP-3,8,9,10 were significantly higher compared with patients with NEDA or without relapses. MMPs did not correlate with EDSS variation.

Conclusion: 1) During NAT treatment, MMP-3 and MMP-9 decreased significantly; 2) Patients that continued having relapses had higher MMPs despite NAT treatment; 3) MMPs can be used as biomarkers during NAT treatment, higher values determining the persistence of BBB dysfunction; 4) Further studies are required.

Disclosure: This study was supported by the internal research Grant of The University of Medicine and Pharmacy Targu Mures, Grant Number 18/2015.

EP1135

Low levels of vitamin D in multiple sclerosis patients in geographic areas with higher sunlight levels: Association with quality of life

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Background and aims: Vitamin D status is associated with the incidence and prevalence of a variety of neurologic disorders, including multiple sclerosis. Several studies suggest or support that multiple sclerosis has increased prevalence in geographic areas with lower sunlight levels. We aimed to investigate the correlation between vitamin D level and quality of life in patients with multiple sclerosis who were exposed to sunny seasons within one year in western Turkey.

Methods: Vitamin D status is associated with the incidence and prevalence of a variety of neurologic disorders, including multiple sclerosis. Several studies suggest or support that multiple sclerosis has increased prevalence in geographic areas with lower sunlight levels. We aimed to investigate the correlation between vitamin D level and quality of life in patients with multiple sclerosis who were exposed to sunny seasons within one year in western Turkey.

Results: Of 200 multiple sclerosis patients, 185 (92.5%) had lower vitamin D level. Patients reported no side effects during the study. The increase in Vitamin D level from baseline to 12 months was significant ($p < 0.0001$). The improvements remained significant in all categories of MSQOL-54 after the vitamin D administration ($p < 0.001$). According to our results, the longer vitamin D use the higher improvement of quality of life.

Conclusion: This study showed that the prevalence of vitamin D level is still low in geographic areas with higher sunlight levels, and also, when vitamin D deficiency or insufficiency was corrected, there was indeed a positive effect on quality of life of patients.

Disclosure: Nothing to disclose

EP1136

Brief paroxysmal attacks as initial manifestation of multiple sclerosis

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Background and aims: Multiple sclerosis (MS) is characterised by a variety of symptoms. Usually these symptoms persist for a longer period.

There are, however, reports of patients suffering from repeated paroxysmal events lasting seconds to a few minutes, which may not be recognised as a manifestation of MS. In the literature they are referred to as paroxysmal symptoms or attacks, transient neurological events, and paroxysmal demyelinating events. They consist of brief, frequent and stereotyped attacks which may continue for days to months. The frequency varies from one to thirty times daily. Paroxysmal symptoms are most common early in the course of the disease and may even be the initial manifestation of MS.

Methods: Four types of attacks are identified in the literature: painful tonic spasms, dysarthria occasionally associated with cerebellar ataxia, sensory symptoms, and paresis. The attacks are thought to be caused by ephaptic activation of axons within a partially demyelinated lesion in fibre tracts resulting in transverse spreading of neuronal conduction to adjacent anatomical structures.

Results: We present the case of a male patient aged 23 years who was seen with a 3-month history of attacks of tingling around his right ear spreading to his neck and sometimes to his right forearm. This was associated with a sensation of loss of use in his left leg. MRI of the brain and cerebrospinal fluid analysis were consistent with a diagnosis of MS. The symptoms quickly subsided after starting a treatment with dimethyl fumarate.

Conclusion: MS should be considered in the differential diagnosis of transient neurological events.

Disclosure: Nothing to disclose

EP1137

Regional efficacy of fingolimod in relapsing remitting multiple sclerosis

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Background and aims: Fingolimod is approved in England as a second line treatment for highly active relapsing-remitting multiple sclerosis (RRMS). We aimed to evaluate the real world effects of fingolimod in a typical NHS clinical setting (relevant to appropriate prescribing, safety profile and cost-effectiveness).

Methods: Retrospective review of the medical records and MRI scans of RRMS patients on fingolimod for a minimum of 1 year at Brighton and Sussex University Hospitals NHS Trust. Patient demographics, disease duration, Expanded Disability Status Scale (EDSS) and no evidence of disease activity (NEDA) were used as covariates. Findings were compared with FREEDOMS and TRANSFORMS outcomes.

Results: 61 patients, followed-up for a mean of 2.7-years were included. The cohort was slightly older (mean age 43 vs. 36), included a higher proportion of females (85% vs. 65-69%), had longer disease duration (12.5 vs 8 years) and was more disabled (median EDSS 4 vs 3) compared with the trial data. At 1 year 81.35% were relapse-free, similar to the trial data. For the whole follow-up period, NEDA was seen in 57.37% of patients, suggesting some expected waning effect. 14.75% of patients discontinued treatment. Logistic regression was performed to ascertain the effects of age, gender, disease duration and disability on the likelihood of patients responding to treatment. None of these was found to be significant predictors.

Conclusion: The efficacy of fingolimod mirrored the findings from the pivotal trials in a real world cohort with slightly different demographics.

Disclosure: Nothing to disclose

EP1138

Social cognition and quality of life in multiple sclerosis

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Background and aims: A recent meta-analysis outlined that MS patients could experience poor performances in Social Cognition (SC), defined as “the mental operation underlie social interactions” and specifically in Theory of Mind (ToM, the ability to attribute mental states to oneself and to others). This raises the need to evaluate the impact of SC on Quality of Life (QoL). We performed a cross-sectional study aimed at shedding further light on this relationship.

Methods: We collected socio-demographic and clinical data from 37 MS patients. They were tested for neuro-cognition (Brief Repeatable Battery), social cognition (Story-based Empathy Task, further divided in the following subscores: attribution of intentions (SET-IA), emotional states (SET-EA), together with a control condition (SET-CI)), depression, fatigue (Beck Depression Inventory and Fatigue Impact Scale) and QoL (Multiple Sclerosis Quality Of Life-54).

Results: SET global score and SET-IA were not related to any clinic-demographic, cognitive and psychosocial features except for disease duration (coeff. Beta -0.34, p=0.04 and coeff. Beta -0.42, p=0.01 respectively). SET-CI and SET-EA scores were not related to any clinic-demographic, cognitive or psychosocial features. Finally, neither physical composite or mental composite scores were related to SET measures.

Conclusion: Although ToM abilities might be involved in social activities and be related to QoL, this association did not emerge in our sample. Since ToM is the ability to understand others' emotions and intentions and MS patients could have ToM deficits, they could be not completely aware of their emotions and intentions involved in social context making them not impacting on the self-perception of QoL.

Disclosure: Nothing to disclose

EP1139

Translating the Parkinson's Disease Sleep Scale (PDSS-2) into 31 languages using a standardized methodology

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Background and aims: The Parkinson's Disease Sleep Scale (PDSS-2) is a patient self-rating scale comprising 15 items, evaluated on a 5-point frequency scale, which assesses nocturnal disturbances in Parkinson's disease (PD) patients. The objectives of this study are to present the method and the challenges of the PDSS-2 translation (originally developed and validated in British English and German) into 31 languages, now widely used in various countries.

Methods: In each country, the translation process consisted of: 1) Conceptual analysis of the original PDSS-2 with its developers; 2) Forward/backward translation step; and 3) Test on five PD patients through interviews. An adjusted process was used for countries using a national variant of the same language (e.g., adaptation of the British English version for use in Australia).

Results: The translation process did not reveal any cultural issues since most of the concepts assessed in the PDSS-2 are cross-culturally relevant. Most of the difficulties belonged to the semantic, pragmatics and syntactic fields. For instance, the word "night" in item 2 (Did you have difficulty falling asleep each night?) could not be literally translated in eight languages. For contextual and colloquial reasons, the word "evening" was more appropriate in Czech, Danish, French (Belgium, Canada, France), Italian, Latvian, and Slovak. The distinction between "sometimes" and "occasionally" in the frequency scale created a range of queries, solved in collaboration with the developers. Other examples are presented.

Conclusion: The multi-step rigorous translation methodology was key in developing 31 translations of the PDSS-2 conceptually equivalent to the British English original.

Disclosure: Nothing to disclose

EP1140

Efficacy of cladribine tablets in patients after conversion to clinically definite multiple sclerosis (CDMS): Analysis of the ORACLE-MS study open-label maintenance period

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Background and aims: In the ORACLE-MS study in patients with a first demyelinating event, cladribine tablets (3.5 and 5.25mg/kg) significantly reduced risk of conversion to clinically definite MS (CDMS) vs placebo. If CDMS occurred in the initial double-blind treatment period (DBTP), patients entered an open-label maintenance period (OLMP) and received interferon-beta 1a. Here, annualised relapse rate (ARR) and lymphopenia during the OLMP of the ORACLE-MS study were assessed.

Methods: Participation in the OLMP depended upon the clinical course of the patient's disease in the DBTP. Patients in ORACLE-MS who converted to CDMS during the DBTP entered the OLMP and received subcutaneous interferon-beta 1a (titrated over 4 weeks to 44mcg) 3 times/week.

Results: 109 ORACLE-MS patients converted to CDMS in the DBTP and received ≥ 1 dose of interferon-beta 1a. Disposition is shown in Figure 1. Median time on interferon-beta 1a was 56.0 weeks. Estimated ARR in the OLMP are shown in Figure 2.

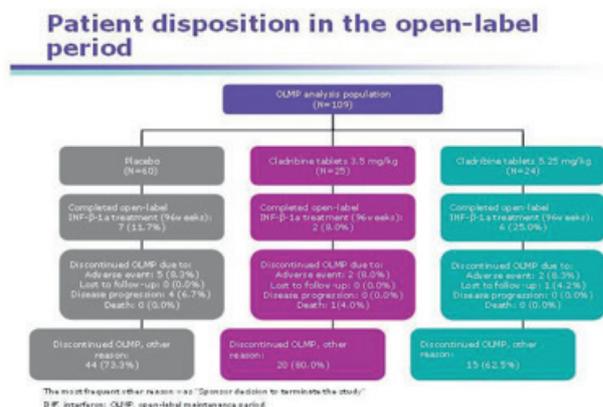


Figure 1

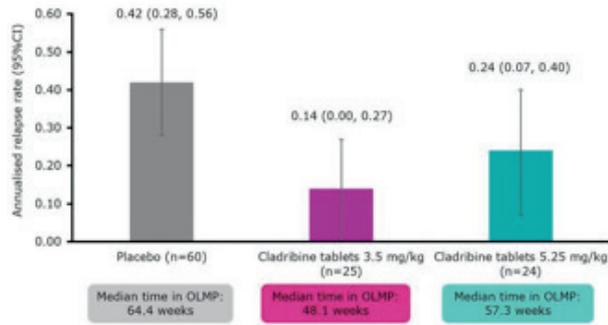


Figure 2

Conclusion: In these exploratory analyses for the open-label maintenance period of ORACLE-MS, treatment effects of cladribine tablets were observed in patients who converted to CDMS and subsequently received sc IFN β -1a. The point estimate of ARR in the open-label period was lower in patients originally randomised to cladribine tablets 3.5mg/kg, compared with placebo. There were no observed differences in MRI activity during the open-label period. The incidence of lymphopenia during the open-label period following conversion to CDMS was low, even if sc IFN β -1a was administered within 10 months of the last dose of cladribine tablets.

Disclosure: This study was funded by Merck KGaA, Darmstadt, Germany. Medical writing assistance was provided by inScience Communications, Springer Healthcare, Chester, UK, and was funded by Merck KGaA, Darmstadt, Germany.

EP1141

Safety of cladribine tablets in the treatment of patients with multiple sclerosis (MS): An integrated analysis from the MS clinical development program

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Background and aims: Efficacy has been demonstrated for cladribine tablets (CT) in patients with early MS and relapsing MS (RMS) in the ORACLE-MS, CLARITY, and CLARITY Extension studies. Adverse event (AE) data from these studies have been reported separately. Pooled safety data for integrated analyses allowing comprehensive characterisation of CT 3.5mg/kg (CT3.5) AE profile are reported here.

Methods: The monotherapy oral 3.5mg/kg cohort comprised 923 patients (3432.65 patient years [PY] exposure) derived from CLARITY, CLARITY Extension, ORACLE-MS and the PREMIERE registry; 641 patients in this cohort received placebo (2025.97 PY; Table 1).

	Placebo (n=641)	Cladribine tablets 3.5 mg/kg (n=923)
Patients	641	923
Time on study (weeks, mean(SD))	194.93 (208.97)	194.49 (208.93)
Time on study (cumulative interval at least 2 years, n (%))	488 (76.1)	773 (83.6)
Time on study (cumulative interval at least 4 years, n (%))	381 (59.4)	688 (74.5)
Age (years), (mean (SD))		
Total	38.8 (9.8)	38.8 (10.8)
Min - Max	18.0 - 64	16.0 - 85
Age 60-69 years, n (%)	418 (65.2)	693 (75.1)
Age 70-79 years, n (%)	228 (35.6)	231 (25.1)
Female, n (%)	317 (49.5)	513 (55.6)
Female, n (%)	424 (66.0)	612 (66.3)
First treatment with CT3.5, n (%)	381 (59.4)	584 (63.3)

SD, Standard Deviation; SD, Standard Deviation; SD, Standard Deviation

Table 1

Results: The mean study period for patients receiving CT was 194 weeks; 165 weeks for placebo recipients. Adj-AE per 100PY rates for CT3.5 and placebo are reported in Table 2. Concerning known events expected with CT treatment, Adj-AE per 100PY for lymphopenia (preferred term) were 7.94 (CT3.5) and 1.06 (placebo), and for system organ class

of infection and infestations, 24.93 (CT3.5) and 27.05 (placebo); herpes zoster (preferred term), 0.83 (CT3.5) and 0.20 (placebo). Adj-AE per 100PY for the system organ class of neoplasms, benign, malignant and unspecified were 1.14 and 1.01, for CT3.5 and placebo, respectively.

Table 2. Adjusted incidence of TSEs

	Placebo (N=411)			Cladribine tablets 3.5 mg/kg (N=422)		
	n	%	Adj-AE per 100PY	n	%	Adj-AE per 100PY
Number of patients with TSE	818	848.2	84.28	772	748.4	108.20
Number of patients with TSE related to study drug	193	1182.8	18.08	840	1809.9	83.78
Number of patients with TSE leading to treatment discontinuation	21	1000.7	1.08	87	3228.0	2.07
Number of patients with serious TSEs	87	1878.8	8.87	124	3088.8	8.00
Number of patients with TSE leading to death	8	2024.7	0.28	9	2481.0	0.28

TSEs was defined as result in death, withdrawal, required inpatient hospitalisation, congenital anomaly or both (defect) or was otherwise considered as medically important in the number of patients with events, *n* is the total patient's time on study in case.

If a patient has multiple events, the time to first event is considered. Here patient with no event the time is censored at the last follow-up time for that patient's TSE, treatment or emergent adverse event.

Table 2

Conclusion: The AE profile for CT3.5 as monotherapy has been well-characterised in a pooled population of patients from early to more advanced RMS. Lymphopenia was expected from cladribine tablets' mode of action; herpes zoster was reported more frequently in patients experiencing Grade 3 or 4 lymphopenia; no clustering of types of malignancy, and no malignancies commonly associated with immunosuppression were observed.

Disclosure: This study was funded by Merck KGaA, Darmstadt, Germany. Medical writing assistance was provided by inScience Communications, Springer Healthcare, Chester, UK, and was funded by Merck KGaA, Darmstadt, Germany.

EP1142

Year-by-year lymphopenia rates in patients with relapsing multiple sclerosis (RMS) treated with cladribine tablets 3.5mg/kg in CLARITY and re-treated in CLARITY Extension

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Background and aims: CLARITY and CLARITY Extension demonstrated the efficacy of cladribine tablets (CT) in patients with RMS. The most common adverse event was lymphopenia, consistent with the mechanism of action of CT. Here we evaluate whether lymphopenia persists following treatment with CT.

Methods: Lymphopenia by grade (Common Terminology Criteria for Adverse Events v3.0) for patients who were randomised to CT 3.5mg/kg in the two-year CLARITY study and re-randomised to CT 3.5mg/kg in the two-year CLARITY Extension (N=186) are reported. Patients with Grade 0 lymphopenia ($\geq 1.0 \times 10^9$ cells/L) before the first course and Grade 0/1 ($\geq 0.8 \times 10^9$ cells/L) prior to administration of all subsequent courses in Years 2/3/4 were included in the analysis, according to re-treatment guidelines.

Results: 176 patients were Grade 0 at the start of CLARITY and 167 patients were Grade 0/1 at the start of CLARITY Extension (Table). By Week 13 in Year 1 and Week 12 in Years 2/3/4, 18–55% of patients developed Grade 2/3 lymphopenia. By Week 48 in each of Years 1/2/3/4, Grade 2/3 was observed in 11–14% (Figure). Occurrence of Grade 3 lymphopenia at any time was reported in <18% of patients; no patients had Grade 4 lymphopenia.

Table: Year-by-year lymphopenia by grade in patients that received cladribine tablets 3.5 mg/kg in CLARITY followed by retreatment in CLARITY Extension

	CLARITY				CLARITY Extension			
	Baseline	End of year 1	Baseline	End of year 1	Baseline	End of year 1	Baseline	End of year 1
Patients*	176	175	161	154	187	161	156	123
Lymphopenia grade [†]								
0	176	119	122	97	134	86	85	59
1	0	37	39	39	33	52	51	48
2	0	19	0	16	0	23	0	16
3	0	0	0	2	0	0	0	0
4	0	0	0	0	0	0	0	0

* Data shown are number of patients.
[†] Patients had lymphopenia Grade 0 at the baseline of Year 1, and Grade 0 or 1 at the baseline of Years 2–4; end of year values are the number of patients with laboratory values.
[‡] Lymphopenia graded by National Cancer Institute Common Terminology Criteria for Adverse Events v3.0

Table 1

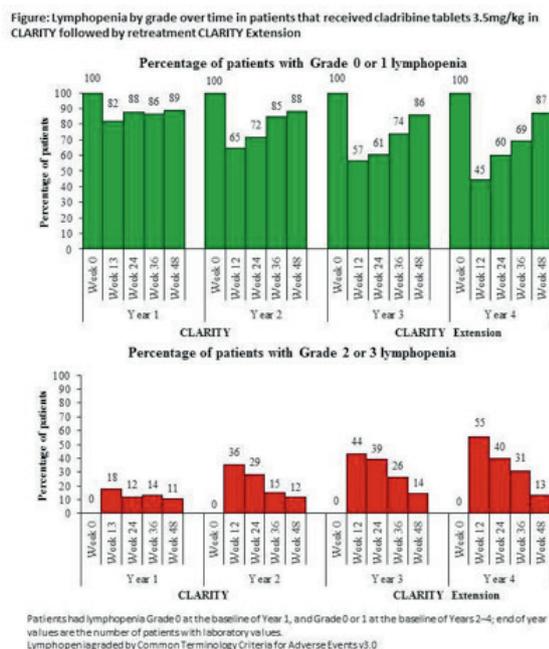


Figure 1

Conclusion: In patients with lymphocyte counts $\geq 1.0 \times 10^9/L$ before the first course and $\geq 0.8 \times 10^9/L$ before ≤ 3 subsequent annual courses of CT, no patients experienced Grade 4 lymphopenia at any time. Approximately 86% of patients recovered to Grade 0/1 by the end of each treatment year. There was no reduction in the proportion of patients recovering towards baseline with additional CT courses.

Disclosure: This study was funded by Merck KGaA, Darmstadt, Germany. Medical writing assistance was provided by inScience Communications, Springer Healthcare, Chester, UK, and was funded by Merck KGaA, Darmstadt, Germany.

EP1143

Fingolimod 2012 and 2016: How did the profile of patients treated with fingolimod change? A comparison of two non-interventional studies PANGAEA and PANGAEA 2.0

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Background and aims: Over the years the therapeutic options for multiple sclerosis (MS) increased and treatment guidelines changed. How did this change the profile of the fingolimod-treated patients from 2012 to 2016?

Methods: PANGAEA and PANGAEA 2.0 are two non-interventional studies conducted in Germany that recruited patients switching to fingolimod between 2011/12/13 and 2015/16 respectively. Here we compare baseline data from these two studies to demonstrate a change in the profile of relapsing-remitting MS patients that switch to fingolimod.

Results: The mean age of patients enrolled in PANGAEA 2.0 was slightly younger (38.4 ± 10.7 vs 38.8 ± 10.1 years) compared with PANGAEA and higher proportion of patients were younger than 40 years (59.6% vs. 54.1%). Patients in PANGAEA 2.0 have a shorter disease history (7.3 ± 6.6 vs. 8.2 ± 6.3 years) a similar number of relapses 12 months before baseline (1.3 ± 1.0 vs. 1.5 ± 1.2), a lower EDSS (2.2 ± 1.6 vs. 3.0 ± 1.7) and MSSS scores (multiple sclerosis severity score; 3.5 ± 2.5 vs. 5.1 ± 2.6). 41.9% of the patients in PANGAEA 2.0 had an EDSS score of ≤ 1.5 at baseline (PANGAEA: 23.3%). The MSSS score of 50.0% of the patients in PANGAEA 2.0 ranged within the first 3 deciles (PANGAEA: 29.5%). 18.2% of the patients in PANGAEA 2.0 were treatment naïve or without any treatment in the previous 12 months (PANGAEA 5.8%).

Conclusion: Patients enrolled into PANGAEA 2.0 (2015/16) switched to fingolimod earlier from a demographic and clinical point of view in comparison with PANGAEA (2012/13). This might indicate a trend towards optimizing fingolimod therapy early in MS from 2012 to 2016 in Germany.

Disclosure: This study was supported by the Novartis Pharma GmbH, Nuremberg, Germany

EP1144

5 years safety of fingolimod in real world: Results from PANGAEA, a non-interventional study of RRMS patients in Germany

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Background and aims: Fingolimod (FTY720; Gilenya[®], Novartis Pharma AG) is approved for the treatment of relapsing MS. As of August 2016, approximately 160,000 patients have been treated with Fingolimod.

PANGAEA (Post-Authorization Non-interventional German sAFETY study of GilEnyA in RRMS patients) is a non-interventional study, conducted in Germany, to investigate long-term safety, effectiveness and patient reported outcomes in daily practice.

Methods: 4229 patients were enrolled into PANGAEA. By Jan 2017 over 300 patients finished the five year documentation period. Here we present safety and adherence data of fingolimod treatment in daily clinical practice for up to five years.

Results: Over five years, the yearly mean study discontinuation rate was 12%. 67% of patients who started fingolimod treatment between 2011 and 2013 in PANGAEA are still on drug. 79% of patients who discontinued the study also discontinued fingolimod. Most frequent reasons for study discontinuation (multiple answers possible) were patient's decision (33%) and adverse events (28%). Over five years, the safety profile of fingolimod in real world is comparable to that observed in phase III clinical trials. Common adverse events were reductions in lymphocyte counts, increase in liver enzyme values, upper respiratory tract infections (e.g. nasopharyngitis [9.9%]), and MS related adverse events like fatigue (3.4%) and depression (2.6%). Approximately 45% of the patients experienced no adverse events. 3.9% of all adverse events were rated as serious.

Conclusion: The results of PANGAEA support the positive benefit-risk profile fingolimod, demonstrated in clinical trials, with real world evidence data. The frequency/nature of reported adverse events is consistent with previous findings.

Disclosure: This study was supported by the Novartis Pharma GmbH, Nuremberg, Germany.

EP1145

Teriflunomide real-world outcomes in the phase 4 Teri-PRO Study: Results from Europe, Canada, and Latin America

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Background and aims: Teriflunomide is a once-daily oral immunomodulator for relapsing-remitting MS. Teri-PRO (NCT01895335), a global, phase 4 study in patients with relapsing forms of MS, investigated patient-reported outcomes (PROs), effectiveness, safety, and tolerability associated with teriflunomide treatment in routine clinical practice in the US and rest of the world (Europe, Canada, and Latin America; ROW). Here, we report outcomes for Teri-PRO patients enrolled in ROW.

Methods: ROW patients received teriflunomide 14 mg for 48 weeks. The primary outcome was patient Global Satisfaction at Week (W)48, measured using the Treatment Satisfaction Questionnaire for Medication (TSQM-V1.4). TSQM scores were measured at baseline (patients switching from a prior disease-modifying therapy [DMT]), and at W4 and W48/end of treatment. Secondary outcomes included PRO assessments, annualized treated relapse rate, and adverse events (AEs).

Results: For ROW patients (n=455), mean (SD) age was 42.9 (10.1) years; time since first MS symptoms was 11.3 (8.9) years. TSQM Global Satisfaction remained high over the study period (mean [95% CI]: W4, 72.3 [70.4, 74.2]; W48, 68.5 [66.0, 70.9]). In patients switching from another DMT (n=278), mean (95% CI) Global Satisfaction significantly improved from baseline (54.9 [51.9, 57.8]) to W48 (70.4 [67.4, 73.4], P<0.0001). Mean treated relapse rate was low (0.23). AEs were reported in 385 (84.6%) patients, and were mostly mild to moderate.

Conclusion: High levels of treatment satisfaction with teriflunomide were observed in ROW patients, including significant improvements in patients switching from another DMT, consistent with the full study population. Teriflunomide was well tolerated and safety outcomes reflected those observed in other studies.

Disclosure: Study supported by Sanofi Genzyme.

MS and related disorders 2

EP1146

Cancelled

EP1147

Retrospective evaluation of hospitalizations in a cohort of multiple sclerosis patients from a tertiary centreA. Costa¹, C. Maia², M.J. Sá¹, P. Abreu¹¹Neurology, Centro Hospitalar de São João, Porto, Portugal, ²Faculty of Medicine of University of Porto, Porto, Portugal

Background and aims: There is poor knowledge on current hospitalizations in the multiple sclerosis (MS) population. Our aim is to examine hospitalization causes and outcomes in a MS cohort.

Methods: Retrospective study of MS patients admitted to our Centre between August 2009 and July 2015, excluding admissions to establish MS diagnosis.

Results: There were observed 308 hospitalizations from 155 patients with MS, mainly women (67.5%), with a median age of 47 (IQR 23). Relapsing-remitting MS was present in 51.1%, the overall median Expanded Disability Status Score (EDSS) was 4.5 (IQR 5) and the median MS duration was 12 years (IQR 10). Infection was responsible for 22.1% of hospitalizations and diseases of the nervous system for 21.4% (including 59.1% due to relapses but also epilepsy, tremor and others). They were followed by diseases of the genitourinary (14%) and circulatory systems (9.7%) and neoplasms (6.8%). A total of 23 hospitalizations (7.5%) required Intensive Care (IC) admission. The length of stay and death rate were higher in patients requiring IC. There were no significant differences in age, gender, MS duration, disease subtype, comorbidities or EDSS in those needing IC. Nine admissions (2.9%) resulted in death. IC admission, secondary progressive MS and increased comorbidities index (Charlson index) were statistically related to fatality.

Conclusion: Infections are the most common cause of hospitalizations in our study. Almost 8% of all MS hospitalizations required IC admission. These may be related to longer admission lengths and higher death rates. Mortality may be associated with secondary progressive MS, comorbidities and IC admission.

Disclosure: Nothing to disclose

EP1148

On the possible role of kappa free light chain index (KFLCi) in the initial setting for the diagnosis of multiple sclerosisI. Crespi¹, R. Serino¹, E. Saliva², M. Marchiando², A. Mora², D. Vecchio³, C. Comi³, R. Cantello³, G. Bellomo¹¹Clinical Chemistry Laboratory, Azienda Ospedaliera-Universitaria Maggiore della Carità Novara, Novara, Italy,²Clinical Chemistry Laboratory, Azienda Ospedaliera-Universitaria Maggiore della Carità Novara, Novara, Italy,³Institute of Neurology, University of Eastern Piedmont, Novara, Italy

Background and aims: Diagnosis of multiple sclerosis (MS) includes clinical and imaging findings to demonstrate lesions dissemination in space and time and to exclude other diseases. The contribution of biochemical assays of cerebrospinal fluid (CSF) is marginal. However, the kappa free light chain index (KFLCi) has emerged as alternative marker, with high sensitivity and low costs.

Methods: 85 patients were enrolled in this preliminary study: 54 had a suspicion of MS (sMS) and 31 of non MS Inflammatory Disease (sNMSID) within the central nervous system. MS diagnosis was based on the 2010 McDonald's criteria (MD). KFLCi has been measured on serum and CSF by nephelometry.

Results: 34 sMS patients (63%) fulfilled both the MD criteria at clinical presentation and had a KFLCi above cut-off values (5); all of them were diagnosed as MS. Despite 20 sMS patients (37%) did not fulfill MD criteria, a final diagnosis of MS was confirmed in 13 of them (65%). In the 92% of this latter group, KFLCi was indeed above the cut-off value. About 23% of sNMSID patients fulfilled the MD criteria at the time of rachicentesis and had a KFLCi higher than 5; for all of them a final diagnosis of MS has been confirmed. Despite 74% of sNMSID patients initially did not fulfill MD criteria, MS was confirmed in 26% of them, and KFLCi was indeed above the cut-off value in 86% of them.

Groups	Initial suspect diagnosis of MS or NMSID (n)	Final confirmed diagnosis of MS (n)
sMS MD+ KFLCi+	34	34
sMS MD+ KFLCi-	0	0
sMS MD- KFLCi+	13	12
sMS MD- KFLCi-	7	1
sNMSID MD+ KFLCi+	7	7
sNMSID MD+ KFLCi-	1	0
sNMSID MD- KFLCi+	10	6
sNMSID MD- KFLCi-	13	0
Total	85	60

sMS: suspected Multiple Sclerosis

sNMSID: suspected Non Multiple Sclerosis Inflammatory Disease

MD: McDonald Criteria

KFLCi: kappa free light chain index

Suspect and confirmed diagnosis of the patients investigated

Conclusion: These findings strongly suggest that KFLCi must be included in the initial setting to improve diagnosis of MS

Disclosure: Nothing to disclose

EP1149

Time to pregnancy in multiple sclerosis: A case control comparative study

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Background and aims: Multiple sclerosis (MS) is a neurological disease mostly affecting women of childbearing age. The likelihood of spontaneous conception in subsequent cycles is important in MS, mostly because of the indication to withdraw the disease-modifying treatments due to their unknown effect during pregnancy. We used data on the number of cycles required for a couple to conceive (time to pregnancy). Time to pregnancy provides a sensitive measure of fertility.

Methods: A prospective, observational study in a clinical-based cohort of MS patients was performed. Clinical and epidemiological data were analyzed. Numbers of noncontracepting cycles until conception were collected. Data were compared with a healthy age-matched control group.

Results: MS cohort: 56 patients. Relapsing-remitting: 87%, primary progressive 6%, secondary progressive 6%. Disease duration: 9.2 years (2-22). Unintended pregnancies 6%. EDSS at pregnancy 1 (0-5). Time to pregnancy 3.77 month. Infertility treatments: 12%. Control group: 64 women. Unintended pregnancies 12.5% ($P < 0.05$). Time to pregnancy 3.66 month ($P > 0.05$). Infertility treatments: 10%. ($P > 0.05$)

Conclusion: This study reveals that time to pregnancy is similar between MS patients and the control group. A major proportion of unintended pregnancies were found in the control group. The likelihood of conception in subsequent cycles is of major interest to neurologist for a better Disease Modifying Therapies (DMTs) planning.

Disclosure: Nothing to disclose

EP1150

Corpus callosum demyelination associated with acquired stuttering

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Background and aims: Differences have been reported in fractional anisotropy, voxel-based morphology, and white matter integrity in the corpus callosum of patients with developmental stuttering. Adult onset acquired stuttering is uncommon; however, case reports have described callosal infarction and neoplasm associated with acquired stuttering.

Methods: Case Report

Results: A 32-year-old female with polycystic ovarian syndrome presented with fatigue, concentration impairment, and acute headache. Neurological and fundoscopic exam were normal. CSF was normal except for 10 nucleated cells (95% lymphocytes). Immunological testing was not performed. Opening pressure was 31 cm H₂O but performed in a flexed position. Non-contrast brain MRI demonstrated multiple ovoid nonspecific T2 hyperintensities in the subcortical and deep white matter. Migraine or possible IHH was suspected and Topiramate initiated. One month later, the patient gradually developed stuttering and stopped Topiramate. Severity of stuttering progressed, and she developed new bilateral lower extremity paresthesias. Severe stuttering and bilateral thigh numbness were noted on neurological exam, but was otherwise normal. Brain and spinal cord MRI demonstrated new T2 hyperintense lesions, including an enhancing 11 mm x 8 mm lesion in the rostrum of the corpus callosum and a non-enhancing C7-T1 T2 hyperintensity. CSF demonstrated 14 nucleated cells (90% lymphocytes), 10 oligoclonal bands restricted to CSF, elevated IgG index, and normal opening pressure. The patient was diagnosed with MS, started on disease modifying therapy, and speech impairment slowly improved over the following 3 months.

Conclusion: Corpus callosal lesions are a common radiographic finding in multiple sclerosis but uncommonly affect language. In rare cases, callosal demyelination may be associated with acquired stuttering.

Disclosure: Nothing to disclose

EP1151

Evoked potentials and other guiding factors of conversion from radiologically isolated syndrome to definite multiple sclerosis

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Background and aims: Radiologically Isolated Syndrome (RIS) has become a popular subject recently with quite number of follow-up and other clinical studies being done. The aim of our study was to assess the role of VEP and SEP as a guiding factor for the conversion from RIS to MS.

Methods: 49 RIS patients who were referred our Neurology department between 2011-2015. All of the patients fulfilled the Okuda criteria. For the VEP examination the p100 latency and amplitudes, for the SEP examination the p40 latency and amplitude was analysed.

Results: 49 patients were included in this study, the mean time of follow up was 21.8 months. 63% of patients were female. The mean age was 31.2 years. Among the 4 patients with abnormal SEPs, MS developed in 3 of them (75%) over time ($p:0.011$) VEP and/or SEP was abnormal in 8 patients and MS develops in 4 (50%) ($p:0.017$). The most important factor for the transformation is the presence of active plaque with increases the risk 8.1-fold. The second important factor seems to be the presence of VEP and/or SEP abnormality, but this factor does not reach statistical significance.

Conclusion: In this conversion to MS risk from RIS, VEP-SEP examinations are important and should take its place in the follow-up of these patients.

Disclosure: Nothing to disclose

EP1152

Characterising immunological properties of dimethylfumarate treatment: Longitudinal data from MS patients

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Background and aims: The mode of action of dimethylfumarate (DMF), an immunomodulatory treatment for relapsing-remitting multiple sclerosis (RRMS), has not yet been fully elucidated. While in-vitro experiments suggest effects on pathways essential for immune cell survival, cytokine secretion and oxidative stress response, a proof from human ex-vivo studies is lacking.

Methods: Blood samples were collected from twenty well-characterized RRMS patients at baseline and after 3 months of DMF treatment and an age- and gender-matched cohort of healthy individuals at 0 and 3 months. Peripheral blood mononuclear cells (PBMC) were separated and cryopreserved for flow cytometry and immunoassays. Lymphocyte subpopulations and cytokine patterns were recorded. PBMC were assessed for their response to oxidative stress induced by hydrogen peroxide, their T cell proliferative capacity as well as activation of NFkB and MAPK pathways.

Results: After 3 months DMF treatment T cell counts dropped by 31 percent with increasing CD4/CD8-ratio, while other lymphocyte populations were not altered significantly. No change in response to oxidative stress was detected. DMF inhibited proliferation of T cells ($CD8 > CD4$), but this anti-proliferative effect decreased over time. Both ex-vivo and in-vitro treatment with DMF resulted in altered cytokine profiles; specifically secretion of interleukin 4 and interleukin 6 was reduced after 3 months. Longitudinal data on NFkB and MAPK activation in lymphocytes will be presented.

Conclusion: This study expands the knowledge on alterations in lymphocyte patterns and translates in-vitro and ex-vivo findings on DMF related immune response and pathway activation into the clinical setting.

Disclosure: This study was supported by an Investigator Initiated Trial grant from Biogen. The institution (University Hospital Basel) received in the last 3 years and used exclusively for research support: steering committee, consulting and speaker fees from Actelion, Addex, Bayer HealthCare, Biogen, Biotica, Genzyme, Lilly, Merck, Mitsubishi, Novartis, Ono, Pfizer, Receptos, Sanofi-Aventis, Santhera, Siemens, Teva, UCB and Xenoport; support of educational activities from Bayer HealthCare, Biogen, CSL Behring, Genzyme, Merck, Novartis, Sanofi-Aventis and Teva; royalties from Neurostatus Systems GmbH; grants from Bayer HealthCare, Biogen, the European Union, Merck, Novartis, Roche, the Swiss Multiple Sclerosis Society and the Swiss National Research Foundation.

EP1153

Antibodies against MOG for patients with neuromyelitis optica and neuromyelitis opticus spectrum disordersJ.L. Frederiksen¹, S. Sandvik²¹Rigshospitalet - Glostrup and University of Copenhagen, Glostrup, Denmark, ²Department of Neurology, Rigshospitalet - Glostrup, Glostrup, Denmark

Background and aims: Neuromyelitis optica (NMO) and NMO-spectrum of disorders (NMOSD) are inflammatory disorders of the central nervous system (CNS). The detection of anti-AQP4-antibodies (AQP4Abs) has become an important part of the diagnosis, but in some patients AQP4Abs cannot be detected even if the patients are clinically similar and the diagnosis is the same. This group of NMO/NMOSD patients is called sero-negative. Myelin oligodendrocyte glycoprotein (MOG) is a surface protein of the myelin sheath in CNS. We investigated if anti-MOG-antibodies may play a role as a diagnostic marker for NMO/NMOSD making it relevant to define a new sero-positive NMO/NMOSD subgroup.

Methods: Systematic searches were performed in PubMed, Cochrane library and Scopus for original articles regarding ON or NMO/NMOSD antibodies against MOG were analyzed.

Results: We found 158 MOGAb+ accounting for 16% of NMOSD patents. This group distinguished itself phenotypically from AQP4+ patients by being younger, have a more equal gender distribution, more often being monophasic, with fewer and less severe attacks and better disorder resolution. They could, however, not account for all AQP4Ab- NMOSD patients.

Conclusion: MOGAb+ NMOSD patients distinguish themselves phenotypically from AQP4Ab+ patients, but cannot account for all the AQP4Ab- patients with NMOSD. MOGAb are found in several other demyelating CNS disorders and are thus not specific for NMOSD. It remains to reveal if the presence of MOGAb is a marker for a distinct underlying mechanism of disorder with phenotypical characteristics comprising multiple of today's established diagnosis. Further research is needed to establish such a potential mechanism, for example to determine the right treatment.

Disclosure: Nothing to disclose

EP1154

Smoking: Effects on the progression of Multiple Sclerosis - a cohort study of patients treated with immunomodulatory therapyV. Crone¹, J.L. Frederiksen²¹Rigshospitalet - Glostrup, Glostrup, Denmark, ²Rigshospitalet - Glostrup and University of Copenhagen, Glostrup, Denmark

Background and aims: We investigated the influence of smoking on disease progression measured by Expanded Disability Status Scale (EDSS) in patients with Multiple Sclerosis (MS) treated with immunomodulatory therapy (IMT).

Methods: We conducted a retrospective national representative cohort study on all consecutive treated patients with MS and Glostrup University Hospital. Data on smoking habits was collected on 871 patients (632 women and 239 men). Kruskal-Wallis One Way Analysis of Varians was used and results were adjusted for age at onset, gender, and disease duration.

Results: The results showed no significant association between smoking and disease progression measured as change in EDSS score/years of treatment ($p=0.196$). Smokers ($n=236$) tended to have a higher initial and final EDSS score (p -value 0.056 and 0.085, respectively).

Conclusion: We found no correlation between smoking and disease progression in patients treated with IMT. The results contribute to the still open debate whether smoking affects the progression of MS. The results suggest that smoking cessation may be less important for patients treated with IMT, but further studies are needed.

Disclosure: Nothing to disclose

EP1155

Quantitative MRI in daily practice: Assessment of brain volume and lesion load in patients with multiple sclerosis from INSPIRATION study

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Background and aims: To investigate the results of standardised MRI-scans qualitatively and quantitatively, obtained from patients with MS. INSPIRATION, a non-interventional multicentre study conducted in Germany, aimed to validate the feasibility and explore the potential benefits of standardized MRI-acquisition and centralized quantitative MRI-reading in clinical practice for RRMS patients.

Methods: INSPIRATION included 253 patients from 15 centers between 05/2014 and 07/2015. MRI and clinical data will be documented over 3 years. Staff at individual sites underwent expert training and standardized sequence implementation. A centralized quantitative MRI-data analysis was performed. The results were reported to the neurologist and radiologist.

Results: 99.6% of the obtained MRI-scans passed the quality analysis; <0.03% of scans led to site inquiries or data exclusion. The mean number (+/-SD) and volume (+/-SD) of T2-lesions at baseline was 30.1(+/-2.8)/11033.1(+/-1578.9)mm³ and that of black holes was 4.0(+/-0.9)/490.3(+/-136.6)mm³. The corresponding values after 12 months follow-up were 32.3(+/-3.6)/11479.9(+/-1927.5)mm³ and 4.1(+/-1.1)/488.9(+/-165.2)mm³, respectively. Whole brain volume at baseline was 1,142,397(+/-15,988)mm³. Brain volume reduction after 12 months was 3,231(+/-1,944)mm³ (0.28%+/-0.1%).

Conclusion: Comparability of MRI-Scans is a central medical need in the management of MS patients. INSPIRATION provides a centralized quantitative MRI-analysis and might improve the comparability of individual MRI-scans in daily clinical routine. The quantification of lesion volumes and visualization of MRI-abnormalities may facilitate neurologists to integrate MRI-data to support patient management.

Disclosure: This study was supported by the Novartis Pharma GmbH, Nuremberg, Germany.

EP1156

High Disease Activity (HDA) definitions in patients with Relapsing Multiple Sclerosis (RMS) receiving placebo in the CLARITY Study

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Background and aims: The 2-year CLARITY study in patients with RMS allows assessment of HDA definitions for identifying patients with a higher rate of relapse or disability progression.

Methods: Placebo recipients in CLARITY (N=437) were retrospectively analysed using two sets of HDA criteria that assessed whether they had experienced high relapse activity ([HRA] ≥ 2 relapses in the previous year) regardless of prior treatment, or HRA plus treatment nonresponse ([HRA+TNR] ≥ 2 relapses in the previous year OR ≥ 1 relapse in previous year while on DMD therapy and ≥ 1 T1 Gd+ or ≥ 9 T2 lesions). The ability of these criteria to identify HDA patients among placebo recipients was assessed according to relapse and disability outcomes.

Results: ARR was higher in the placebo HRA and the placebo HRA+TNR subgroups than in the overall placebo population and the non-HRA and non-HRA+TF subgroups (Figure 1). Time to first qualifying relapse was shorter in the HRA and HRA+TF subgroups than the overall placebo population and the non-HRA and non-HRA+TNR subgroups. Time to 6-month confirmed EDSS progression (10% of patients) was 110 days for the HRA subgroup (non-HRA patients=330 days), 162 days for the HRA+TNR subgroup (non-HRA+TNR patients=329 days) and 245 days, overall placebo population (Figure 2). The increased ARR and shorter time to EDSS progression highlights the increased risk in patients identified by these HDA criteria.

Figure 1. ARR in placebo recipients by HDA subgroup

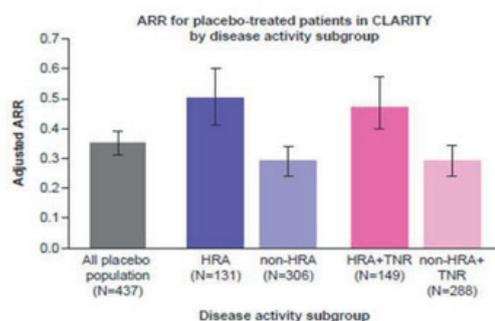


Figure 1

Figure 2. Kaplan-Meier survival curves for time to 6-month EDSS progression by HDA subgroup

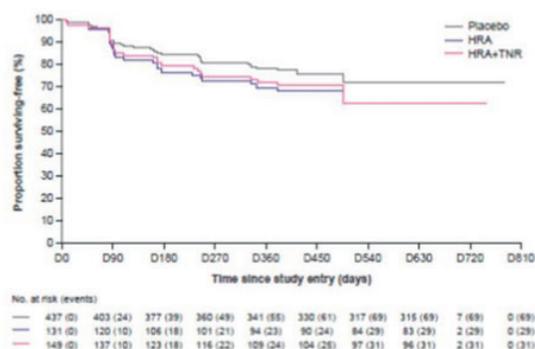


Figure 2

Conclusion: Post-hoc analysis from the CLARITY study showed that HDA criteria based on relapse history, treatment history and MRI characteristics can identify patients with RMS at increased risk of experiencing relapses and disability progression.

Disclosure: This study was funded by Merck KGaA, Darmstadt, Germany. Medical writing assistance was provided by inScience Communications, Springer Healthcare, Chester, UK, and was funded by Merck KGaA, Darmstadt, Germany.

EP1157

Cladribine tablets in high disease activity (HDA) subgroups from the CLARITY study of patients with relapsing multiple sclerosis (RMS)

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Background and aims: In the CLARITY study, treatment with cladribine tablets (CT) vs placebo showed strong efficacy in a large cohort of patients with RMS over 2 years. Patients with HDA are at higher risk of relapses and disability progression. This post-hoc analysis compared the effects of CT 3.5mg/kg (CT3.5) vs placebo in subgroups of CLARITY patients selected using two HDA definitions.

Methods: CLARITY patients randomised to CT3.5 (N=433) or placebo (N=437) were retrospectively analysed using two different HDA definitions based on relapse history, prior treatment, and MRI characteristics. Patients were categorised according to whether they had experienced high relapse activity ([HRA] ≥ 2 relapses in the previous year) regardless of prior treatment, or HRA plus treatment nonresponse ([HRA+TNR] ≥ 2 relapses in the previous year, or ≥ 1 relapse in previous year while on DMD therapy and ≥ 1 T1 Gd+ or ≥ 9 T2 lesions).

Results: In the overall CLARITY population, CT3.5 reduced the risk of 6-month confirmed EDSS progression by 47% vs placebo (Figure 1). A larger risk reduction for CT3.5 vs placebo of 82% was seen in the HRA subgroup and the HRA+TNR subgroup indicating greater responsiveness to CT3.5 in patients identified by these criteria. ARR was lower with CT3.5 than placebo in the overall population and even lower with for the HRA and HRA+TNR subgroups (Figure 2).

Figure 1. Forest plot of Hazard Ratio of time to 6-month confirmed EDSS progression by HDA subgroup for cladribine tablets 3.5 mg/kg vs placebo

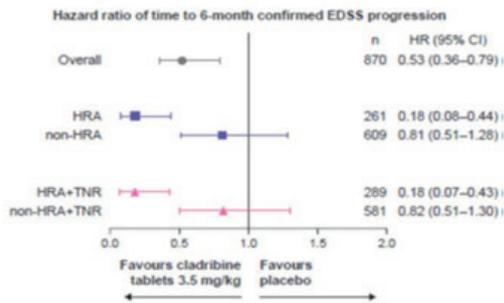


Figure 1

Figure 2. Forest plot of Relative Risk of ARR by HDA subgroup for cladribine tablets 3.5 mg/kg vs placebo

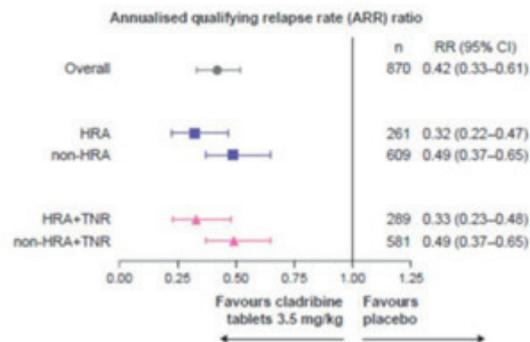


Figure 2

Conclusion: In the CLARITY study, patients identified by HDA criteria showed clinical and MRI responses to CT3.5 that were generally better than, or at least comparable with, the outcomes seen in the overall CLARITY population.

Disclosure: This study was funded by Merck KGaA, Darmstadt, Germany. Medical writing assistance was provided by inScience Communications, Springer Healthcare, Chester, UK, and was funded by Merck KGaA, Darmstadt, Germany.

EP1158

Investigation of demographic and clinical properties of familial multiple sclerosis patients

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Background and aims: Multiple sclerosis (MS) is known as an autoimmune neurodegenerative disease, characterized by familial aggregation. In this study, it was aimed to investigate the familial transition characteristics of MS, thereby contributing MS genetics studies and helping with personalized therapy approaches.

Methods: We investigated 110 patients (admitted to MS outpatient clinic between January 2015 - November 2015) from 50 families - with members that were diagnosed with definitive MS diagnosis according to the 2010 McDonald criteria - in terms of demographical and clinical properties.

Results: Paternal inheritance was observed on the 19 of the patients and maternal inheritance was observed on the 30 of all the patients. When the relatives of the patients with paternal and maternal transition observation was compared, significant difference was found ($\chi^2=6.437$, $p=0.04$). Median EDSS (2015) value was 3.0 (1.5 – 6.0) and median MSSS value was 3.4 (1.6 – 6.4) for all patients involved in the study. Median MSSS value for paternal transition observed patients was determined to be 1.6 (0.6-2.9) and for maternal transition observed patients was 4.5 (2.1 – 6.7); and the difference was significant ($p=0.016$; $z=-2.411$).

Conclusion: This study shows that clinical presentation and progression is more severe in maternally inherited MS cases compared to paternally inherited MS cases. Thus early diagnosis and treatment is important however, larger and more homogenous patient cohorts, prospective controlled studies would be more helpful in deciding treatment options and management.

Disclosure: Nothing to disclose

Muscle and neuromuscular junction disease 1

EP1159

Ephedrine and 3,4 daminopyridine responsive myasthenic syndrome in plectin-related epidermolysis bullosa simplex with muscular dystrophy

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Background and aims: Mutations in the plectin gene causes a variety of disorders, namely: epidermolysis bullosa simplex with muscular dystrophy (EBS-MD), EBS-MD with myasthenic features (EBS-MD-MyS), limb girdle muscular dystrophy type 2Q, EBS with pyloric atresia, and EBS-Ogna. We report an unusual patient with EBS-MD-MyS, who displayed a marked suppression of his myasthenic symptoms in response to ephedrine and 3,4 daminopyridine (3,4-DAP).

Methods: No

Results: A 41-year-old Caucasian male suffered from congenital hypotonia, muscle weakness, delayed motor milestones, and skin and mucous membrane blistering since birth. At the age of 25, he developed progressive symmetrical scapular and peroneal weakness and atrophy. In his early thirties, additional ptosis, diplopia, dysphagia, and fatigue manifested. CK-levels were markedly elevated (2,200-16,000 UI/L). Needle EMG showed a generalised myopathic pattern, and repetitive nerve stimulation studies at 3 Hz depicted a 20% decremental response. MRI showed pronounced fatty replacements of shoulder girdle muscles, the posterior compartment of thighs, and the anterior compartment of his legs. Muscular biopsy revealed severe dystrophic changes and desmin-positive aggregates. Genetic analysis revealed two heterozygous PLEC mutations: one (c.11737del; p.(Arg3913Valfs*30)) leading to a premature translational stop codon, and a second (c.2539-2A>G) residing in the highly conserved splice-acceptor site of intron 21. While pyridostigmine was of no benefit, a combination of ephedrine and 3,4-DAP effectively controlled his myasthenic-related symptoms.

Conclusion: To date, no specific treatment is available for any form of plectinopathy. In EBS-MD patients with additional evidence of myasthenia, a combination of ephedrine and 3,4-DAP should be considered as a symptomatic treatment option.

Disclosure: Nothing to disclose

EP1160

Cancelled

EP1161

Exercise-induced fatigue and measurement of oxidative stress biomarkers in myotonic dystrophy type 1 DM1

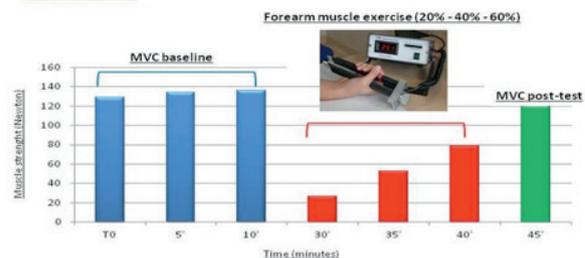
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Background and aims: Fatigue, the inability to maintain the expected motor performance over time, can be an acute or chronic status in neuromuscular disorders; a greater fatigability it is reported to be more common in myotonic dystrophy (DM1) (Laberge et al. 2009). Oxidative stress has been proposed to be one of the pathogenic factors (Angelini and Tasca, 2012), although others (Bray et al. 2012) suggested a role for CNS involvement.

Methods: We studied exercise-induced fatigue in a sample of adult-onset DM1 patients (17males, 9females, mean age 41.6yrs, sd±12.7), through an intermittent-incremental-effort-exercise; oxidative stress balance blood biomarkers were collected. Motor disability was assessed using a muscle impairment rating scale (MIRS). To test for possible effects of central fatigue, patients have been administered with clinical scales about fatigue, mood and quality of life.

STUDY DESIGN



Results: Our exercise protocol proved to be easily deployable and well-tolerated. Statistical analysis revealed a significant increase in AOPP in DM1 patients versus controls but no significant differences between oxidative stress balance markers before and after the effort (Fig.2-3). The occurrence of central fatigue suggests that central activation worsens during motor contractions; central-fatigue score(FSS) was significantly correlated to MVC (r-before: -0.583, p<0.01; r-after=-0.534, p<0.05), and to motor disability (r-MRC =-0.496, p<0.05).

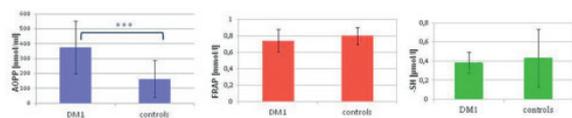


Figure 2. Plasma levels of AOPP (A), FRAP (B), total thiol groups (C) in DM1 patients vs controls (CTL). *** p<0,001.

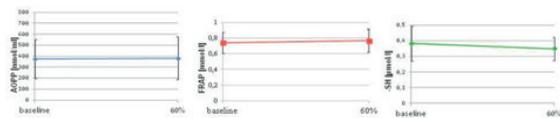


Figure 3. Changes in plasma levels of AOPP (A), FRAP (B), total thiol groups (C) in DM1 patients. *** p<0,001.

Conclusion: Biochemical correlates of oxidative stress represent a viable biomarker for clinical use in, although these markers still need to be validated in larger sample sizes; these results also suggest that comparative studies assessing CNS and muscle involvement are useful to define fatigability profile in DM1.

Disclosure: Nothing to disclose

EP1162

Towards a definition of fatigability profile in myotonic dystrophy type 1 (DM1)

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Background and aims: Myotonic dystrophy type 1 (DM1) is characterized by high fatigability (Kalkman et al. 2005). Oxidative-stress (Angelini and Tasca, 2012) and central mechanisms (Bray et al. (2012)) have been proposed to be possible pathogenic factors. Our aim was to investigate the fatigability profile in DM1, looking specifically at the relationship between self-reported fatigue, objective measures of peripheral fatigue, cognitive performance and gross brain structure.

Methods: We studied fatigability profile in a sample of 20 adult-onset DM1 patients (14 males, 6 females, mean age 41.6 years, sd±12.7) through an intermittent incremental effort (Sogaard et al. 2006). To test for effects of central fatigue, patients have been administered fatigue severity scale (FSS), cognitive tests and 3T magnetic resonance (MR) imaging.

Results: FSS-score was significantly correlated to MVC before and after the effort, ($r_{\text{before}}=-0.583$, $p<0.01$, $r_{\text{post}}=-0.534$, $p<0.05$), and to motor disability ($r=-0.496$, $p<0.05$); moreover we found a strong tendency trend-to-significance in the association with baseline-lactate ($r=0.378$, $p=0.057$). Out of the six measures of cognitive performance used, 40% (n=8) of DM1 patients had impairment in two or more scores related to attention processes. MR imaging investigations revealed that DM1 patients had reduced gray-matter volume in the bilateral prefrontal cortex, consistently with previous studies reporting this area to play a role in the neural regulation of fatigue.

Conclusion: These data suggest that fatigue in DM1 is a multifaceted entity, also related to the disruption of fatigue-related processes in the brain. The tools used in this study may be used as effective means to define fatigability profile in DM1 patients.

Disclosure: Nothing to disclose

EP1163

Clinical, laboratory and anatomopathological evaluation of patients with RyR1 mutations

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Background and aims: Mutations in the RyR1 gene underlie several debilitating and/or life threatening muscle conditions: central core disease, susceptibility to malignant hyperthermia, multiminicore disease and centronuclear myopathy.

To describe the clinical, laboratory, anatomopathological and genetic findings of a group of patients with RyR1 gene mutations followed at the Neuromuscular Disease Unit of the Neurology Department of Coimbra's University and Hospital Center.

Methods: The medical files of patients with confirmed RyR1 mutations were reviewed for demographic, historical and clinical data. Serum creatine kinase, forced vital capacity, electromyography and muscle biopsies were also analysed.

Results: Seven patients, three females, from five unrelated families were included. There was no parental consanguinity. The symptoms began in childhood or the second decade of life and were very slowly progressive. All patients acquired independent ambulation but three had a delayed attainment of motor skills. One patient, son a symptomatic patient, was asymptomatic. Five had proximal upper and lower limb weakness and one only proximal lower limb weakness. One patient presented with malignant hyperthermia. The mean value of CK was 1111.25UI/L. The muscular biopsies showed characteristics of central core disease (two), multiminicore disease (one) and centronuclear disease (one). All patients had a molecular study confirming the existence of a pathogenic variant in the RyR1 gene.

Conclusion: Our study provides further evidence that RyR1 related myopathies are very heterogeneous. Clinical, histopathological and molecular features are essential to better understand genotype-phenotype correlation.

Disclosure: Nothing to disclose

EP1164

20 years clinical follow-up in patients with oculopharyngeal muscle disease (OPMD)

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Background and aims: Oculopharyngeal muscle dystrophy (OPMD) is an autosomal dominant muscle disease. OPMD is clinically characterized by ptosis, eye movement abnormalities, dysphonia and dysphagia. It is caused by an abnormal (GCN) triplet expansion within the PABPN1 gene located on chromosome 14 (14q11.2-q13).

Methods: We present a cohort of 18 patients (12 female and 6 male) with OPMD. We performed quantitative Electromyography in all patients and muscle biopsy in 11 out of 18. We also applied MRC score for muscle strength evaluation as well as the EAT-10 (Eating Assessment Tool) which is a self-administered scale for dysphagia evaluation. All patients were genetically defined for PABPN1 gene variants.

Results: Main results are shown in table 1.

Dysphagia and dysphonia worsened during the course of the disease as well as orbicularis oculi muscle strength; in addition, we observed that either axial muscles or posterior thigh muscles were progressively affected. 10 patients were evaluated with EAT-10 showing a worsening of dysphagia.

table 1

Pt	Sex	Age	Family size	Onset symptoms	Q-EMG	CK	Muscle biopsy	Orbicularis oculi MRC onset	MRC last visit	AM last visit	PTM last visit
1	F	55	no	ptosis, dysphonia	normal	↑	normal	3	4	4	4
2	F	50	yes	ptosis	em-opathic	↑	atrophy, some	4	4	4	3
3	M	60	no	ptosis, dysphonia, dysphagia	em-opathic	↑	rimmed atrophy	4	3	4	3
4	M	55	yes	dysphagia, ptosis	normal	↑	atrophy, some	4	4	4	5
5	F	40	yes	ptosis, OP	normal	↑	normal	4	3	5	5
6	M	50	yes	ptosis, dysphagia, dysphonia	normal	↑	ND	4	3	4	5
7	F	50	yes	ptosis, OP, dysphagia	normal	↑	ND	4	4	4	5
8	M	56	yes	ptosis, dysphagia	em-opathic	↑	atrophy	4	4	5	5
9	F	60	yes	ptosis	normal	normal	atrophy, some	4	3	4	5
10	M	44	yes	ptosis, OP, dysphagia	em-opathic	normal	atrophy	4	3	4	3
11	F	46	yes	dysphagia	normal	normal	ND	4	4	5	4
12	M	45	yes	ptosis, dysphagia	normal	normal	ND	4	4	5	5
13	F	60	yes	ptosis, OP	normal	normal	atrophy	4	4	5	5
14	F	55	yes	asymptomatic patient	normal	normal	ND	5	5	5	5
15	F	55	yes	ptosis, OP	normal	normal	atrophy, some	4	4	5	5
16	F	56	yes	ptosis, dysphagia	normal	normal	ND	4	4	4	3
17	F	58	yes	ptosis, dysphagia	em-opathic	normal	atrophy	4	4	5	5
18	F	50	no	ptosis, dysphagia	em-opathic	normal	ND	4	3	3	3

Legend Q-EMG= quantitative electromyography; MRC= Medical Research Council; AM= axial muscles; PTM= posterior thigh muscles; OP= orbital myopathy; RV= rimmed vacuoles; ND= not done

table 1

Conclusion: Our data confirms that, at disease onset, the weaker mimic muscles are the orbicularis oculi. During the OPMD course, it has been found a worsening of orbicularis oculi weakness and of dysphonia and dysphagia with a progressive involvement of proximal limb and axial weakness.

Disclosure: Nothing to disclose

EP1165

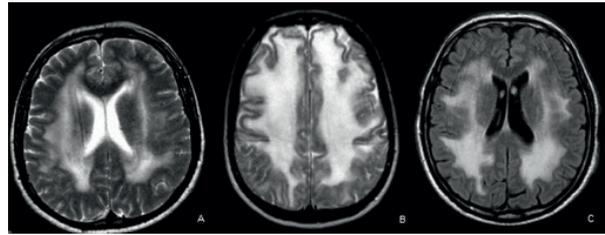
Limb girdle muscular dystrophy due to LAMA2 gene mutations: 5 new Italian cases enlarge the clinical and molecular spectrum of the disease

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Background and aims: Mutations in LAMA2 gene, encoding merosin, are generally responsible for a severe Congenital Muscular Dystrophy (CMD type 1A). Since now only few cases with adult-onset and partial merosin deficiency have been reported.

Methods: We describe 5 independent Italian subjects presenting with Limb Girdle Muscular Dystrophy (LGMD), brain white matter abnormalities, merosin deficiency and LAMA2 gene mutations. Patients underwent complete neurological examination, muscle biopsy, brain and muscle imaging.

Results: All patients showed slowly progressive proximal weakness with onset spanning from childhood to adulthood. Creatin-kinase levels were moderately elevated. One patient developed dilated cardiomyopathy. Muscle MRI allowed to evaluate the degree and pattern of muscular involvement in all patients. Brain MRI was fundamental in order to direct and/or support the molecular diagnosis, showing typical widespread white matter hyperintensity in T2-weighted sequences in all subjects; these alterations were associated with signs of central nervous system (CNS) involvement in 3 patients presenting epilepsy (2) and migraine (1). Muscle biopsy showed heterogeneous patterns ranging from dystrophic to myopathic features; misleading patterns were also detected, leading to the suspect of mitochondrial myopathy and polymyositis. Protein analysis displayed partial merosin deficiency. LAMA2 gene analysis detected 7 different mutations, 6 of which are new.



Brain MRI - Axial TSE T2 images (A-B) and axial T2 FLAIR images (C) showing diffuse abnormal hyperintensity involving peri- and sovra-ventricular white matter in three different patients.

Conclusion: These cases further enlarge the clinical spectrum of LGMD due to mutations in LAMA2 gene. In our opinion this form is an underestimated cause of LGMD and CNS study, which was fundamental to address the diagnosis, should be included in the diagnostic workup of undiagnosed LGMD.

Disclosure: Nothing to disclose

EP1166

Cancelled

EP1167

Congenital myasthenic syndrome with favourable response to 4-aminopyridineD. Cerdan¹, B. Fernandez¹, C. Simonet², J. Eguizábal¹, A. Castrillo¹, J. Duarte Garcia Luis¹¹Neurology, Hospital Complex of Segovia, Segovia, Spain,²Neurology, Clinic Hospital, Barcelona, Spain

Background and aims: Congenital Myasthenic Syndromes (CMS) are infrequent inherited disorders, difficult to diagnose, with several clinical features, in which neuromuscular transmission is compromised by different mechanisms. We present a patient with a CMS caused by a mutation in the epsilon subunit of acetylcholine receptor (AChR), who has a surprising clinical response with 4-aminopyridine (4-AP), although not approved in Spain for this use. 4-AP is reportedly effective in refractory cases of CMS.

Methods: A 27-year-old female who was diagnosed a CMS when she was 3. She presented generalized weakness and ophthalmoplegia, and she was treated with pyridostigmine, ephedrine, fluoxetine and salbutamol with incomplete beneficial effects. In 2015, a mutation in gene CHRNE was found, after doing a genetic panel. Because of different treatments inefficacy, she was offered an off-label agent, 4-AP. She was treated with oral 4-AP (20mg/day) for up to 10 months. We supposed it could have some effect in prolonging the action potential by blocking potassium channels, and consequently, increasing calcium entry into the nerve terminal. Similar to 3,4-diaminopyridine, it could have positive effects in structural defects of the AChR subunit.

Results: She obtained a rapid and extremely good clinical response, which is still maintained, improving her quality of life.

Conclusion: MCS have some thoroughly known effective medications, as pyridostigmine or 3,4-diaminopyridine. Nevertheless, in many patients the beneficial effects are incomplete and other therapeutic options are limited because of the absence of controlled clinical trials. 3-AP could be a symptomatic treatment in some CMS. It is needed to continue researching about such findings.

Disclosure: Nothing to disclose

EP1168

Still looking for predictors for myasthenic crisis occurrenceV. Deneva¹, M. Milanova²¹Neurology, Alexandrovska University Hospital, Sofia, Bulgaria, ²St Naum University Hospital, Sofia, Bulgaria

Background and aims: Myasthenic crisis (MC) is a complication of Myasthenia gravis (MG), characterized by increase of muscle weakness which results in respiratory failure and requires intubation and mechanical ventilation or non-invasive ventilation. The latest medical strategies are focused on prevention of myasthenic exacerbation/crisis, including evaluation and early managing of the precipitating factors. In this study we evaluate the significance of different precipitating factors for aggravation of MG resulting in MC, describing a cohort of 97 Bulgarian patients with autoimmune myasthenia, of whom 26 presenting crisis. The listed factors were stress, infection, surgery, pregnancy, therapy changing or aggravation of another persisting disease. Since we had discovered that important part of MC are caused by unknown precipitating factor, we evaluated the significance of other concomitant conditions such as depression, thymectomy, presence of hypertension or other autoimmune disease.

Methods: Statistical analysis was performed using two-sided tests at a significance level of $\alpha=0.05$, and for each factor an Odds ratio (OR) was calculated.

Results: The results show that the major precipitating factor for crisis development is infection with OR7.44 (CI95% 2.01-27.54; $p<0.05$). The factor influence of depression over the crisis development was significant in our group with OR7.181 (CI95% 2.258-22.830; $p<0.001$), as well as for thymectomy with OR4.297 (CL 1.454-12.699; $p=0.001$). All other evaluating factors did not show a significant correlation to MC occurrence.

Conclusion: The presence of infections, depressive disorders and thymectomy may exhibit a higher predictive significance for MC occurrence and applying specific preventive strategies is needed.

Disclosure: Nothing to disclose

EP1169

Long-term follow-up and IgG anti rh-GAA assessment in late-onset Pompe disease

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Background and aims: Late-onset Pompe disease (LOPD) is an autosomal recessive metabolic disorder due to deficiency of the lysosomal acid alpha-glucosidase enzyme. In 2006, alglucosidase alfa (rhGAA) was approved as an enzyme replacement therapy (ERT) for Pompe Disease. Efficacy of ERT in LOPD has been well demonstrated. However, only few studies have assessed ERT effects in long-term treated patients and the role of IgG anti rh-GAA antibodies in modulating efficacy of treatment is still incompletely known.

Methods: We report clinical and functional findings from 9 LOPD patients treated with ERT for a time ranging between 3 and 9.5 years. Serial measurements of IgG anti rh-GAA antibodies were performed in 7 of them.

Results: At the end of observation, respiratory function tests improved or were stable in 66% of cases; the walked distance at 6MWT improved in 75% of the patients up to 54 months, while in the subsequent follow-up (up to 108 months) 63% of them slowly reduced the walked meters. MRC subscore shows stabilization or improvement in 88% of patients. Titers of anti-rhGAA antibodies also in very long treated patients are only mildly elevated (max 12800). No clear-cut relation between titers of anti-rhGAA antibodies and clinical outcome were observed.

Conclusion: Our results confirm ERT long-term effectiveness, though it appears to be reduced over time compared to the first two years of therapy.

A specific relation between titers of anti-rhGAA antibodies and response to treatment seems not to exist but it deserves further studies on wider numbers of patients.

Disclosure: Nothing to disclose

EP1170

International-DMD (IDMD): A PTC therapeutics-supported diagnostic project to widely identify dystrophin mutations by NGS technologies

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Background and aims: Extensive molecular diagnosis in genetic diseases is vital to confirm clinical diagnosis and to enable genetic counseling and personalized management. Duchenne muscular dystrophy (DMD) is a rare genetic neuromuscular disease affecting 1/5000 males, due to a variety of dystrophin gene mutations. The first signs and symptoms of DMD include delayed milestones such as walking and talking, and enlarged calves. PTC Therapeutics International Ltd. and the University of Ferrara, Italy, have established a collaboration focused on identifying patients affected by rare genetic disorders through increased genetic testing activities, with an initial focus on DMD. Genetic testing is available to patients throughout European countries, potentially expanding to other regions.

Methods: Diagnostic settings include MLPA (MRC Holland) and NGS dystrophin gene sequencing (Multiplicom).

Results: Currently DNA from 57 DMD boys was collected. Patients were from Poland (34), Hungary (10), Lithuania (5), Romania (3), Russia (1) and Serbia (4). Among the 30 samples analyzed, 7 deletions, 4 duplications, 11 small mutations (8 nonsense) were identified.

Conclusion: This collaborative project demonstrates PTC's commitment to expanding awareness of the importance of genetic testing for patients with DMD. The early identification of the underlying genetic mutation is critical to potentially affecting the course of a disease such as DMD as well as the choice of treatment and aids in the setup of appropriate and effective care and follow up. Genetic counselling can also be offered to patients and families with important repercussions on reproductive choices and lifestyle planning (full details and contacts at www.ospfe.it/medicalgenetics).

Disclosure: Work supported by PTC Therapeutics International Ltd.

EP1171

Cancelled

Neuroimmunology 1

EP1172

Plasma exchange for neurological disorders in Hungary – an overview of 10 year's data in the NEUROHUN 2004-2013 projectD. Bereczki¹, A. Ajtay¹, F. Oberfrank²¹Department of Neurology, Semmelweis University, Budapest, Hungary, ²Institute of Experimental Medicine, Hungarian Academy of Sciences, Budapest, Hungary

Background and aims: Plasma exchange (PE) may be the preferred intervention due to financial considerations in some neuroimmunological diseases where intravenous immunoglobulins could also be applied as an evidence-based treatment. We evaluated the use of PE in a 10-year period in Hungary.

Methods: Hungary has a single-payer health insurance system covering the whole population of 10 million inhabitants. In the framework of the Hungarian Brain Research Program we created the anonymized NEUROHUN database from medical reports submitted for reimbursement purposes to the National Health Insurance Fund from all hospitals and outpatient services throughout the country for the ten-year period between 2004 – 2013. ICD-10 codes were used for diagnoses. Clinical diagnoses of the patients with PE treatment were analyzed.

Results: In this 10-year period 8757 persons were treated with PE in Hungary, of these 5127 had some neurological service use and 2586 were given a neurological diagnosis within 10 days of the PE treatment. The vast majority of PE treatments were applied in 3 major diagnostic groups: diseases of the peripheral nervous system (ICD-10 G60–G64, n= 1415), diseases of the myoneural junction (G70–G73, n=836) and demyelinating disorders of the central nervous system (G35-37, n=278).

Conclusion: As in Hungary PE is the preferred method of treatment in Guillain-Barré syndrome (GBS) and chronic inflammatory demyelinating neuropathy (CIDP), the average annual PE treatments in the G60-G64 diagnostic group suggests that the combined incidence of GBS and CIDP may be not less than 1.4/100.000 inhabitants/year in Hungary – corresponding to values reported from other European countries.

Disclosure: Nothing to disclose

EP1173

Hypertrophic pachymeningitis of autoimmune/inflammatory etiologyM. Calejo¹, G. Cação¹, P. Bettencourt Medeiros², T. Mendonça², J.E. Alves³, R. Taipa⁴,N.M.D.S. Vila-Chã¹, A. Martins Silva¹, J. Damasio¹¹Neurology, Centro Hospitalar do Porto - Hospital de Santo António, Porto, Portugal, ²Internal Medicine Department, Centro Hospitalar do Porto - Hospital de Santo António, Porto, Portugal, ³Neuroradiology, Centro Hospitalar do Porto, Porto, Portugal, ⁴Neurology Department and Neuropathology Unit, Centro Hospitalar do Porto - Hospital de Santo António, Porto, Portugal

Background and aims: Hypertrophic pachymeningitis (HP) is characterized by localized or diffuse thickening of the dura mater, with or without inflammation. Different etiologies are recognized, with autoimmune/inflammatory conditions increasingly reported.

Aims: Describe a cohort of HP patients with probable autoimmune/inflammatory etiology.

Methods: Retrospective study. Patients' identification through a key-word search of MRI reports from July/2008-September/2015. Data collection and analysis of those with an autoimmune/inflammatory etiology.

Results: Forty patients with HP were identified, 8 with an inflammatory/autoimmune etiology. Of these, 6 were female, with mean age at clinical presentation of 49.7±12.4 years. Four patients were diagnosed with IgG4-related HP. The remaining were associated with Wegener's granulomatosis (1), sarcoidosis (1), rheumatoid arthritis (RA) (1) and Tolosa-Hunt syndrome (1). In 6 patients PH was the clinical presentation of the underlying inflammatory disease, being only a late manifestation in the patient with sarcoidosis. Presenting symptoms were cranial nerve palsies (3), headache (2), cognitive deterioration (2), lumbar pain (1). PH was cranial in seven patients and spinal in one. Laboratory findings included hiperIgG4-emia (4), raised ECA (1) and serum positivity for pANCA/MPO (1), FR/anti-CCP (1) and ANA (1). Two patients had brain biopsy. Seven patients were treated with corticosteroids, 3 requiring additional immunosuppressants. Overall, outcome was good, with only one relapsing.

Conclusion: In our series of autoimmune/inflammatory PH there was a higher percentage of IgG4-related disease than reported, probably due to increased awareness of this entity. Clinical presentations were diverse, being brain MRI crucial in establishing PH diagnosis. We highlight the importance of laboratory findings in the final diagnosis, and the good outcome of most patients.

Disclosure: Nothing to disclose

EP1174

Thoracolumbar pachymeningitis causing bilateral subacute radicular compression in Wegener's granulomatosis: A case report

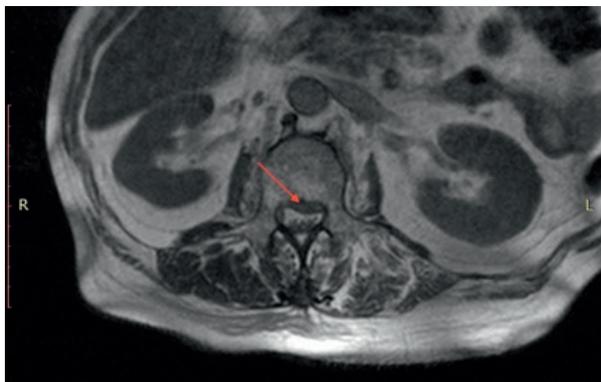
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Background and aims: Spinal dural involvement is one of the least frequent neurologic manifestations of Wegener's granulomatosis (WG).

Methods: We report a case of thoracolumbar pachymeningitis in a patient with a 5-year history of WG. A comprehensive search of the English language literature was performed. The differential diagnosis is widely discussed.

Results: A 70-year-old female presented with subacute paraparesis accompanied by severe lumbar pain and moderate biological inflammatory syndrome in the absence of fever. At age 65 she was diagnosed WG based on histopathological proven bilateral retro-orbital granulomas and aneurysms. Her disease also included pulmonary, rhinosinusitis, uveitis and intracranial dural involvement. The serum titer of proteinase 3 anti-neutrophil antibodies was highly positive. Monthly high-dose cyclophosphamide and corticosteroids applications resulted in remission after 6 months. The MRI scan of the spine showed T11-L3 gadolinium-enhancing dural thickening consistent with WG-related spinal pachymeningitis. The L2-L3 vertebral disc and L3 vertebral body appeared to be mildly involved. Surgical biopsy and decompression could not be performed because of an unexpected fatal cardiac complication probably caused by WG.



Axial T2-weighted spine MRI showing dural thickening at L2 level.



Sagittal pre- and post-gadolinium T1-weighted spine MRI showing the contrast enhancing spinal dural thickening. Mild signal changes and contrast enhancement are also seen in the cranial region of the L2 vertebral body.



Axial post-gadolinium T1-weighted brain MRI showing intraocular and orbital granulomas as well as temporal dural thickening and contrast enhancement.

Conclusion: Meningeal involvement occurs in less than 4% of people with WG. Though very rarely described, isolated spinal dural involvement may be the first manifestation of a WG relapse. Considering the lack of pathognomonic features an infectious cause should be excluded prior to therapeutic immunosuppression.

Disclosure: Nothing to disclose

EP1175

Neurexin-3alpha antibody-associated encephalitis after Plasmodium falciparum malaria

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Background and aims: A new form of autoimmune encephalitis associated with neurexin-3alpha antibodies was recently described in 5 patients. One of them had history of malaria a few months before presentation (not reported). We describe a new case that was preceded by Plasmodium falciparum malaria.

Methods: Review of clinical information. Determination of neurexin-3alpha antibodies was performed as reported (Neurology 2016;86:1-8).

Results: A 57-year-old Caucasian man with no clinical history of interest returned to Portugal after a long stay in Angola. Five days later he was diagnosed with P. falciparum malaria (8% parasitemia) and successfully treated with quinine-doxycycline. Two weeks after recovery he developed fever, somnolence, confusion and abnormal behavior. At examination he was disoriented in time and had inattention, acalculia, and visuospatial difficulties without focal deficits; the general exam was normal. The CSF showed 159 cells (91% mononuclear), protein 2.12 g/dL, and normal glucose. The EEG was consistent with a severe subcortical encephalopathy without epileptic activity. Brain MRI showed a mild increase of T2/FLAIR signal in the caudate-capsule-lenticulate regions without gadolinium enhancement. Extensive CSF and serum studies were negative for infectious or systemic autoimmune causes. On the 8th day, a clinical diagnosis of post-malaria neurological syndrome was made and a 5-day course of 1g intravenous methylprednisolone was initiated with progressive clinical improvement. CSF and serum samples were then found to be positive for neurexin-3alpha antibodies.

Conclusion: The case of this patient suggests that the encephalitis associated with neurexin-3alpha antibodies can develop as post-infectious encephalitis. Recognition of this disorder is important because it responds to immunotherapy.

Disclosure: Nothing to disclose

EP1176

Bickerstaff brainstem encephalitis following Chlamydomphila pneumoniae infection

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Background and aims: Bickerstaff's brainstem encephalitis (BBE) is a rare entity characterized by acute ophthalmoplegia, ataxia, altered consciousness, and variable signs of central nervous system dysfunction. It is included in the "anti-GQ1b antibody syndrome" along with a spectrum of disorders with a common immunological profile and variable overlapping features. Most patients have a history of preceding infection and several causative organisms have been described.

Methods: We report a case of BBE following Chlamydomphila pneumoniae infection.

Results: A 30-year-old patient was admitted to the emergency department with a 24-hour history of gait unsteadiness, ascending weakness and psychomotor retardation. She reported symptoms of an upper respiratory infection a week earlier. Over the next few hours she developed blurred vision, worsening paralysis and became increasingly lethargic. Examination revealed a low-grade fever, drowsiness, bilateral external ophthalmoplegia and facial weakness, dysarthria, and tetraparesis with upper limb hyperreflexia. A diagnosis of BBE was considered and she was admitted to an intensive care unit, requiring assisted ventilation. Cerebrospinal fluid studies showed mild lymphocytic pleocytosis and brain magnetic resonance was normal. Serum anti-GQ1b IgG antibodies were positive, confirming the diagnosis, and a positive C. pneumoniae antigen was detected in bronchial secretions and assumed to be responsible for the respiratory illness. She was treated with intravenous immunoglobulin and doxycycline and slowly improved.

Conclusion: To the best of our knowledge, this is the first report of BBE following C. pneumoniae infection, although this pathogen has been previously reported in cases of MFS and acute isolated ophthalmoplegia. Further studies are needed to clarify a possible causal relationship.

Disclosure: Nothing to disclose

EP1177

Autoimmune limbic encephalitis in an Algerian population: A case seriesA. Djellaoui¹, N. Attal², E. Attal¹¹Neurology, Ait Idir Hospital, Algiers, Algeria, ²Immunology, Institut Pasteur Algérie, Algiers, Algeria

Background and aims: Limbic encephalitis (LE) results in the acute or subacute appearance of a clinical syndrome associating memory disorders, epileptic seizures and / or psychiatric disorders. It may be paraneoplastic or not, pure or associated with an extralimbic involvement. To study the clinical, radiological and immunological profiles of autoimmune ELs associated with anti-neural antibodies in a series of 4 patients. Describe the peculiarities of these EL in our patients and confront atypical situations, not or little reported, to the data of the literature

Methods: A monocentric, retrospective study of ALE associated to onconeural (ONA) and anti-membrane antibodies. All patients received clinical and neuropsychological evaluation, cerebral MRI, standard EEG, infectious, endocrine and metabolic assessment, ONA and membrane epitope antibody (LGI-1 and Caspr2, NMDA-R and GABA_B-R) and finally a primary cancer assessment.

Results: Four patients, all men, aged between 48 and 77 (mean=58.7 years) were included. Clinical, radiological, biological and immunological characteristics are described in Tables 1 and 2

Conclusion: The characteristics of ELAs diagnosed in our patients are:

1. Anti-PNMA 2 LE mimicking Gayet-Wernicke encephalopathy
2. Anti-NMDA-R antibodies following HSV-1 encephalitis
3. LE to anti-Yo in a man, mimicking a Creutzfeldt-Jacob disease
4. The presence of at least one second antibody when the 1st antibody has an intracellular epitope

These descriptions confirm the clinical heterogeneity of ALEs and may contribute, with the discovery of new autoantibodies, to a better knowledge of these encephalitis. This first work in Algeria on ALEs raises the interest of a more extensive study in order to better characterize them.

Disclosure: Nothing to disclose

EP1178

Clinical course of LGI1 and CASPR2-antibodies associated limbic encephalitisE. Edwards¹, L. Imbach², A. Lutterotti³¹Zurich, Switzerland, ²Department of Neurology, University Hospital Zurich, Zurich, Switzerland, ³Unispital Zurich, Zurich, Switzerland

Background and aims: Seizures, cognitive impairment and memory loss as well as other central and peripheral nervous system characterize limbic encephalitis. In the past years voltage-gated potassium channel antibody (VGKC-) associated limbic encephalitis has been characterized and further distinct into subgroups. To date only few case reports have shed light to course and treatment of this devastating disease.

Methods: We would like to present 8 patients with VGKC associated limbic encephalitis (3 of which have VGKC/LGI1- antibodies, 3 present VGKC/CASPR2-antibodies and 2 are VGKC positive but lack both LGI1/CASPR2 antibodies). We will present the clinical course and evolution under immunomodulatory as well as anti-epileptic and psychoactive therapy backed by diagnostic follow up through serum/CNS -serology, magnetic resonance imaging and video-electroencephalogram-findings, detailed neuropsychological testings and additional electrophysiological testing.

Results: Although the case number is limited we would like to help further differentiate those three VGKC-subgroups formally summarized by VGKC-complex-antibodies.

Conclusion: The three VGKC associated limbic encephalitis have distinct patterns of differentiation both in clinical and in diagnostic evaluation. Awareness in clinical presentation as well as serum/CNS -serology, magnetic resonance imaging, electroencephalography and neuropsychological testing can help in early diagnosis and management of this devastating disease.

Disclosure: Nothing to disclose

EP1180

Anti-GAD encephalitis presenting with non-epileptic choreo-dystonic movements and coexisting electric seizures

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Background and aims: Anti-GAD antibodies have been associated with limbic encephalitis, new-onset type 1 diabetes, Stiff-person syndrome, exaggerated startle, cerebellitis, and refractory epilepsy.

Methods: We report a case of a patient with anti-GAD encephalitis including chorea and dystonia.

Results: A 38-year-old woman presented with a 4-month history of involuntary movements of the left hand, slurred speech, and gait instability. On examination, we observed nystagmus and round the houses sign, orofacial dyskinesia, dysarthria, cervical dystonia, choreo-dystonic movements of the left upper limb, and mild gait ataxia. Brain-MRI documented a left temporal hyperintensity in T2 sequence. Anti-GAD title was positive in blood (1/3200) and CSF (1/320). The EEG disclosed nine seizures of left temporal origin in 30 minutes, which showed no temporal correlation with the aforementioned involuntary movements, nor other obvious clinical manifestations. The patient was treated with sodium valproate (1800mg/day), and methylprednisolone, followed by IV immunoglobulin. Upon discharge, she maintained mild orofacial dyskinesia, and choreo-dystonia of the left hand. There were no seizures or interictal epileptiform activity on the EEG and the Jerk-locked back average (JLBA) analysis of the facial movements showed no cortical correlate.

Conclusion: This case of anti-GAD encephalitis presented previously unreported choreo-dystonia, besides electrical temporal seizures. Absence of a cortical correlate of choreo-dystonia on EEG-JLBA, and movement persistence after resolution of the epileptic activity support a non-epileptic origin of those movements. The association of clinical signs of basal ganglia involvement with subclinical electrical seizures expands the spectrum of anti-GAD disorders.

Disclosure: Nothing to disclose

EP1181

Study of inflammation in CSF in NeuroBehçet disease

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Background and aims: NeuroBehçet disease (NBD) is the most frequent vasculitis in our country. In presence of inaugural neurological forms, CSF study is systematic because of diagnosis difficulties.

Our aim was to describe the immunoelectrophoretic and cytokine profile in NBD.

Methods: Criteria of selection: NBD according to the International consensus recommendation (ICR) with definite and probable forms including isolated neurological syndrome suggestive of NBD. Subjects were consecutive patients who referred to Neurological department of Charles Nicolle hospital since 2013. Blood and CSF samples are taken from all patients. Cell counting, protein analysis, immunoelectrophoretic profile with Ig G Index was performed. Cytokines levels were evaluated by PCR.

Results: From 26 NBD recruited 17 had an inaugural neurological form of which 15/17 had a parenchymal involvement. The IgG index was increased in only 2 patients (8%). At the Immunoelectrophoresis, the profile was type 1 in 22 patients (81%), type 2 in 1 patient (3.7%) and type 3 and 4 in 4 patients (11%). The study of lymphocyte populations showed an increase of IL-17, interferon gamma and IL10 levels in more than 80% of patients.

Conclusion: The profile data in CSF of NBD patients in our study are in line with those found in the literature. Given the limited data on CSF levels of cytokines in patients with NBD, our results showed that cytokines make a pivotal role in pathogenesis of NB, as evidenced by the conjoining increase of pro and anti-inflammatory cytokines in our patients.

Disclosure: Nothing to disclose

EP1182

Erythromelalgia and stiff man syndrome: New insights in ion channels pathologyD. Labunskiy¹, V. Poleshchuk²¹Santa Rosa CA, USA, ²Research Center of Neurology, Moscow, Russian Federation

Background and aims: Erythromelalgia (EM) is a rare vascular peripheral pain disorder in which blood vessels, usually in the lower extremities or hands, are episodically blocked. There is severe burning pain in small fiber sensory nerves and skin redness. Stiff person syndrome (SPS) is a disorder characterized by progressive rigidity, stiffness, which affects the truncal muscles, superimposing by spasms. Chronic pain, lumbar hyperlordosis are common. The Nav1.7 voltage-gated sodium channels antibodies (AB) seems to have a cornerstone effect in EM pathophysiology. Glutamic acid decarboxylase (GAD) AB evidently are a positive SPS sign.

Methods: Under our observation were 6 patients with EM and 3 patients with clinically proved SMS. We studied AB against Nav1.7 and GAD in both groups patients and in control group comprising of 34 neurologically healthy donors. Positive labeling by an antibody against the neurofilament protein peripherin was used to identify group IV neurons and axons. Western Blot analysis (WBA) was used to determine concentration of both AB types in these diseases.

Results: Concentrations of AB to Nav1.7 and GAD were considerably increased in all EM with hyperemic and inflamed extremities and SPS patients characterized by spasms and postural deformities, correspondingly. These results were confirmed both by WBA and using immunohistochemistry.

Conclusion: In both cases (EM and SPS) appear as autoimmune neurological disorders with evidence of pathogenic role of AB to Nav1.7 in EM and anti-GAD AB in SPS. Immunohistochemistry and WBA showed some correlation to clinical picture of both sufferings and could serve as targets for future therapeutic approaches.

Disclosure: Nothing to disclose

EP1183

An unusual brainstem encephalitis associated with anti-glycine receptor antibodies: Clinicopathological descriptionD. Lux¹, G. Kumar¹, T. Webb², I. Bodi³, N. Moran¹¹Neurology, Kent & Canterbury Hospital, Canterbury, United Kingdom, ²Neurology and Stroke, Kent & Canterbury Hospital, Canterbury, United Kingdom, ³Neuropathology, King's College Hospital, London, London, United Kingdom

Background and aims: Glycine receptor (GlycR) antibodies are most frequently associated with the syndrome progressive encephalomyelitis with rigidity and myoclonus. Previous reports of GlycR-associated syndromes demonstrated a variable response to immunotherapy. Neuropathological reports are few. The current case is of interest in that it was characterised predominantly by brainstem features without rigidity, responded to immunotherapy and proceeded to post-mortem examination.

Methods: A well 64-year-old man presented with external ophthalmoplegia, facial weakness, bulbar dysfunction, hyper-reflexia and myoclonus with onset three days after coryzal symptoms. There was no rigidity, cognitive impairment or seizures. No neoplastic or vasculitic condition was identified. Serum GlycR antibodies were positive. Negative tests included: onconeural antibodies; antibodies vs. N-methyl-D-aspartate receptor, voltage gated potassium channel, glutamic acid decarboxylase, and gangliosides; MRI of the neural axis; cerebrospinal fluid analysis; nerve conduction studies.

Results: Despite two courses of intravenous immunoglobulin, he had a respiratory arrest and required prolonged invasive ventilation, complicated by fluctuating tachy-bradycardia with intermittent asystole. Following plasma exchange and corticosteroids, he was weaned from ventilation and began mobilising. Ophthalmoplegia and myoclonus completely resolved but bulbar recovery was incomplete. The patient died following severe pulmonary oedema 110 days after presentation. Detailed post-mortem examinations found no significant abnormalities in the brain, spinal cord or heart and no evidence of a malignancy.

Conclusion: This case illustrates a GlycR-associated brainstem syndrome with significant autonomic involvement as well as the potential for neurological improvement with immunotherapy. The absence of rigidity was unusual. The lack of histopathological change supports previous literature arguing against a destructive pathogenesis of GlycR-associated syndromes.

Disclosure: Nothing to disclose. Please include following as reference for abstract: 1. Glycine receptor antibodies in PERM and related syndromes: characteristics, clinical features and outcomes. Carvajal-González A et al. Brain (2014) 137 (8): 2178-92.

Neurorehabilitation

EP1184

Effect of functional electrical stimulation (FES) on the muscle tone and the motor function of the paretic upper limb in four chronic stroke survivors

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Background and aims: To determine whether FES can contribute to inhibit spasticity in the flexor muscles of the affected wrist and improve the motor function of the paretic upper limb.

Methods: The design of the research was a case study. The four patients included in the current study were evaluated before and after 20 sessions of FES (five days a week, for four weeks). Each patient performed several training tasks in the workstation assisted by the FES device. The following parameters were evaluated: (i) the muscle tone of the flexor muscles of the wrist of the affected upper limb, which was measured according to the Modified Ashworth Scale (MAS); (ii) motor function, measured by the Action Research Arm test (ARAT), and (iii) the perception of the manual ability of the paretic upper limb by the Manual Ability Measure -16 (MAM-16).

Results: There was a favourable decrease in the MAS scores in the four participants after the FES intervention. Likewise, there was also an improvement in the ARAT scores and a significant increase in the self-perception of the manual ability of the upper paretic limb after FES intervention.

Conclusion: The application of FES can contribute to manage the spasticity of the flexor muscles of the affected wrist in chronic stroke survivors. In addition, 20 sessions of FES are associated with an improvement in the motor function and the self-perception of the manual ability of the paretic upper limb.

Disclosure: Nothing to disclose

EP1185

Effect of hiding view of the starting hand position when using a home-friendly treatment for spatial neglect in healthy participants

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Background and aims: Prism adaptation is an experimental treatment for spatial neglect with limitations preventing its clinical application. Peg-the-Mole (PTM) is a new home-friendly prism adaptation iPad procedure that induced after-effects in healthy participants. The purpose of this study was to examine whether hiding view of the starting hand position during PTM would increase the magnitude of after-effects by reducing self-correction in pointing movements.

Methods: Sixty healthy participants were randomly assigned to one of four conditions (Goggles: Prism/Sham, Starting Hand Position: Visible/Hidden). After-effects were measured using a proprioceptive and visual pointing tasks and a wheelchair obstacle task.

Results: Larger pointing errors were observed in the Prism/Hidden than the Prism/Visible groups during PTM. Significant Goggles x Starting Hand Position interactions were observed on the visual pointing task and the wheelchair task. The difference in after-effects between Prism and Sham groups on the visual task was larger in the Hidden than the Visible groups ($p < 0.05$). On the wheelchair task, fewer hits on the right side of the course ($p < 0.05$) and a trend for more hits on the left side of the course ($p = 0.06$) were found in the Prism compared to the Sham conditions, but only for the Hidden group.

Conclusion: These results suggest that hiding view of starting hand position contributes to induce larger after-effects by reducing self-correction in pointing movements, which is of clinical relevance considering the relation between after-effects and the improvement in neglect symptoms.

Disclosure: Work supported by Harrison McCain Foundation and Atlantic Innovation Funds.

EP1186

Comparative effectiveness research of dual-task and single-task balance training on gait speed and cognition in individuals with stroke

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Background and aims: Decrements in dual-task capacity may predispose stroke survivors to risk of falls. There is a need to explore whether dual-task training would enhance dual-task performance. The purpose of this study is to compare the effect of single- and dual-task training on gait speed and cognition in stroke patients.

Methods: Twenty-six subjects with stroke were randomly allocated to either a single- or dual-task balance group. Both groups received training at progressively increasing task difficulty (60 minutes per session, three times a week, for four weeks). Single-task group undertook balance and gait training. Dual-task group trained balance and gait while simultaneously performing cognitive tasks. All participants were examined walking and cognition under single- and dual-tasking at pretreatment, posttreatment, and 1-month follow-up. Primary outcome measures of walking and cognition were gait speed and composite score of cognitive tasks (serial 3 subtractions, Stroop, and auditory Stroop) under single- and dual-tasking. Dual-task costs were calculated.

Results: Both groups showed statistically significant improvements on gait speed under single- and dual-task walking, and reduced gait costs under walking with serial 3 subtractions. Compared to single-task group, dual-task group was significantly reduced more gait speed cost under walking with Stroop task at follow-up. Only dual-task group significantly improved gait costs under walking with Stroop and auditory Stroop tasks at posttreatment and follow-up. Both groups significantly improved composite scores of single- and dual-auditory Stroop task.

Conclusion: The preliminary results showed a favorable trend toward dual-task balance training with greater reduced dual-task costs on gait speed.

Disclosure: This work was supported by the Ministry of Science and Technology (104-2314-B-182-035-MY3) and Chang Gung Memorial Hospital (CMRPD3E0331) in Taiwan.

EP1187

Cancelled

EP1188

Neurotransmitters changes after rTMS treatment in patients with secondary-progressive multiple sclerosis and severe spasticity

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Background: To improve our knowledge about neuroplasticity changes in patients with spasticity we used proton magnetic resonance spectroscopy (H-MRS) of motor cortex before and after navigated repetitive TMS (rTMS) of motor cortex.

Introduction: Our aim was to qualify H-MRS technique in assessment of neurotransmitters changes in patients with secondary-progressive multiple sclerosis (SPMS).

Methods: Twenty three patients (10 males, 13 females, mean age 44.7±11.47 years) with SPMS and lower spastic paraparesis were enrolled in double-blind placebo-control study. Neuroplasticity changes in motor cortex area were investigated before and after two types of rTMS (20 Hz, n=9; intermittent theta burst (iTBS), n=5) or sham stimulation (n=9). We assessed levels of neurotransmitters using simple voxel proton MRS. Voxel was placed in the senso-motorial region. For assessment spasticity level we used Modified Ashworth Scale (MAS), Subjective Evaluation Spasticity Scale (SESS) before and at the end of rTMS sessions, SESS - 2 weeks and 3 months after of rTMS sessions.

Results: We did not recognize significant changes in neurotransmitters level in all groups after rTMS. There was only slight increase of lactate level in 20 Hz group. Patients underwent both types of rTMS showed a reduction of spasticity on MAS and SESS in compare with placebo group.

Conclusion: Our results indicate no significant changes in neurotransmitters level after rTMS session in comparison with placebo. But we noticed a significant reduction of spasticity on MAS and SESS in both treatment groups. Lack of H-MRS changes can be due to strong neuroplasticity changes in patients with SPMS.

Disclosure: Nothing to disclose

EP1189

Correlation between cognitive impairment and early functional rehabilitation outcomes after stroke in elderly patients

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Background and aims: Stroke is among the leading causes of disability and mortality in the elderly and leading cause of hospital admission and prolonged length of stay for patients 65 years and older. Evidence from clinical trials supports the premise that early initiation of rehabilitation influences recovery from stroke. Cognitive impairment, as manifested by low scores in mental status questionnaires, has been correlated with limited functional gains and poor rehabilitation outcome in elderly patients.

Methods: Patients and Methods: Our study was prospective and conducted at Neurological department of General Hospital "Prim.dr A. Nakas" Sarajevo during 01.01.2015.-31.12.2015. We included 50 patients older than 70 years hospitalized because of first ischaemic stroke with significant motor impairment which is defined with NIHSS score at admission and at discharge and all of them were included in early rehabilitation program for 2 weeks at Neurological Department. Cognitive status was assessed with the Mini-Mental State Examination (MMSE).

Results: The majority, 69.2%, exhibited cognitive deficits on admission. There were 9.8% patients with an MMSE score equal or lower than 10 points. Better rehabilitation outcomes were observed in patients with higher admission cognitive status, adjusting for the effect of age, sex and severity of stroke (odds ratio 2.57; 95% confidence interval, 1.2–2.5; p=0.01).

Conclusion: Because many rehabilitation techniques require normal cognition and patient cooperation, cognitive status must be considered when determining the rehabilitation aims, establishing treatment strategies and predicting outcome. Better functional outcomes being achieved in cognitively intact elderly stroke patients.

Disclosure: Nothing to disclose

EP1190

Action observation training effects on brain structural and functional changes in Parkinson's disease patients

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Background and aims: To assess brain functional and structural changes following action observation training (AOT) associated with exercises of balance, gait, transfers and manual dexterity in Parkinson's disease (PD) patients.

Methods: Twelve PD patients were randomized into two groups: AOT-group performed a 4-week training consisting of AO combined with practicing the observed actions; LANDSCAPE-group performed the same exercises combined with landscape-videos observation. At baseline (T0) and week 4 (W4), patients underwent clinical assessments. 3D T1-weighted, diffusion tensor (DT) MRI and functional MRI (fMRI) were acquired. fMRI tasks consisted of hand anti-phase movements and motor imagery of circumstances representing activities of daily living. Clinical evaluations were repeated at 3-month follow-up.

Results: At W4 both groups showed changes of the step frequency. The AOT group had an improvement of quality of life at W4 and velocity during manual activities at 3 months. During the hand anti-phase task, AOT-group showed an increased activity of frontal areas and a decreased recruitment of cerebello-thalamo-cortical network, while the LANDSCAPE-group had an increased activity of the thalamus and a decreased recruitment of parietal areas. During the motor imagery task, AOT-group showed a reduced recruitment of the cerebello-thalamo-cortical network and occipital areas, while the LANDSCAPE-group showed an increased activity of motor areas. Only in the AOT-group, functional plasticity was correlated with clinical improvements. AOT-group showed an increased integrity of cerebellar peduncles correlated to cerebellar functional plasticity.

Conclusion: The combination between physical and cognitive exercises has the potential to stimulate both functional and structural brain plasticity compared to a pure motor training in PD patients.

Disclosure: Nothing to disclose

EP1191

Cancelled

Neurotoxicology & Neurotraumatology & Spinal cord and root disorders

EP1192

Cancelled

EP1193

Cancelled

EP1194

Acute neck pain in mild traumatic brain injury as a predictor of chronic posttraumatic complaints

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Background and aims: The role of acute neck pain as a predictor of persistent posttraumatic complaints after mild traumatic brain injury (mTBI) is unknown. The aim of this study was to describe the characteristics and course of acute neck pain following mTBI and its relation to persistent posttraumatic complaints and functional outcome. We also studied whether demographic and injury related factors were associated with persistent neck pain.

Methods: We analyzed data of 933 mTBI patients (n=162 mTBI patients with acute neck pain and n=771 without acute neck pain) admitted to the Emergency Department (ED), from a prospective follow-up study in three level-one trauma centers (UPFRONT-study). Posttraumatic complaints and resumption of activities were evaluated at six months post-injury using standardized questionnaires.

Results: Patients with acute posttraumatic neck pain were more often female (p=0.002) and younger (41 vs. 46 years p=0.002) compared to controls. No differences regarding CT abnormalities were found. Neck pain correlated with headache, dizziness and nausea in the acute phase (p<0.005). Patients with neck pain had more often motor vehicle accidents (p=0.009) and reported more neck pain pre-injury (p=0.012). Also more neck pain and posttraumatic complaints with lower Glasgow Outcome Scale-Extended scores after six months were present.

Conclusion: Acute neck pain after mTBI is a predictor for the development of persistent neck pain and posttraumatic complaints six months post-injury. Pre-injury neck pain and motor vehicle accidents are factors predisposing for acute posttraumatic neck pain. This suggest that patients at risk for an unfavorable outcome might already be identified at the ED.

Disclosure: This study was funded by the Dutch Brain Foundation (grant no. Ps2012-06).

EP1195

Relationship between a sense of generalized anxiety and occurrence of somatic symptoms in patients after mild traumatic brain injury

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Background and aims: The aim of the study was to investigate the relationship between presence of generalized anxiety at the time of mild head injury and the somatic symptoms occurring 3 months after that incident.

Methods: At the beginning using the Generalized anxiety disorder 7-item scale (GAD-7) we evaluated 97 patients consecutively admitted to the Emergency Department because of mild traumatic brain injury (mTBI) but without pathology in computerized tomography scan and who did not require hospitalization. Based on GAD-7 they were divided into two groups: patients with a high level of anxiety (above 6 points) and patients with a low level of anxiety (equal or less than 6 points). Next, from primary group of 97 patients we assessed 56 of them regarding 7 somatic symptoms by using three points measurement (from "1 - not at all", 2 - "a little" to "3 - a lot") during neurological control examination conducted at least 3 months after brain injury.

Results: Among the group of patients with a high level of anxiety on admission, 78% of them reported at least one somatic symptom which was assessed on 3 points, from which 50% of them notified at least two symptoms with 3 points. The majority of patients (89%) from the second group with a low level of anxiety did not report the somatic symptoms.

Conclusion: GAT-7 scale could be useful as a prognostic tool to select patients after mTBI who are predisposed to develop somatic symptoms, what could be helpful to manage this group of patients

Disclosure: Nothing to disclose

EP1196

Alcohol-related mild traumatic brain injury and outcome in elderly patients at the Emergency Department

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Background and aims: Acute alcohol intoxication (AAI) is associated with a higher risk of mild traumatic brain injury (mTBI) in the overall population. However, the incidence and impact of mTBI due to AAI in elderly patients is unknown. The aim of this study was to describe the characteristics of alcohol related mTBI in elderly patients and to determine the mechanism of trauma and outcome.

Methods: We analyzed data from 388 mTBI patients with an age of 55 years or older (84 AAI vs. 304 non-intoxicated patients) from a prospective cohort study in three Dutch level 1 trauma centers (UPFRONT-study). Injury mechanism and outcome were compared between groups. Posttraumatic complaints and functional outcome were evaluated after 2 weeks and 6 months using standardized questionnaires.

Results: 22% of the elderly mTBI patients was intoxicated with alcohol. There was no significant difference in intracranial traumatic CT findings, Glasgow Coma Scale at admission, frequency of hospital admission and Glasgow Outcome Scale Extended compared to controls. Injury Severity Score was higher in the non-intoxicated group (8.5 vs 6.6 $p=0.036$). Falls were the most common trauma mechanism and even more common in the AAI group (94% vs. 72% $p=0.000$). Patients with AAI mTBI reported less posttraumatic complaints after 2 weeks ($p=0.010$) and 6 months ($p=0.044$).

Conclusion: One in five injuries in our aged mTBI patients was alcohol related and most injuries were due to falls. For clinical practice, it might be necessary to focus more on alcohol and fall prevention strategies in the older population to reduce the incidence of mTBI.

Disclosure: This study was funded by the Dutch Brain Foundation (grant no. Ps2012-06).

EP1197

Neurological complications of regional anesthesia: Two cases illustrating a broad spectrum

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Background and aims: Regional anesthesia procedures are associated with a 1-4/10.000 neurological complication rate. Such complications are varied, and include intracranial hypotension, transient Horner syndrome, myelopathy or radiculopathy. We report two cases that illustrate this broad clinical spectrum.

Results: Case 1: A 31-year-old female patient developed, during cesarean section under epidural anesthesia, symptoms indicating rostral spread of local anesthetics (arterial hypotension and left upper limb paresthesiae). After surgery, a left Horner's syndrome was noted. Head CT with CT Angiography was normal. The clinical picture resolved within six hours. Case 2: A 68-year-old female patient submitted to a knee arthroplasty under combined spinal and epidural anesthesia (L3/L4) remained with a flaccid monoparesis and hypoesthesia of the left lower limb with a D7/8 hemisensory level on the left. Spinal MRI revealed an extensive myelopathy, with ischemic features, occupying the left half of the dorsal and lumbar spinal cord. Recovery was poor and the patient maintained the deficits at discharge.

Conclusion: In Case 1 the sympathetic pathway to the eye was transiently compromised because of the rostral spread of the anesthetics. In Case 2 the exact pathophysiological mechanism remains unknown, but imaging features suggest a venous infarction. These two cases remind us that regional anesthesia is not without risk. The pathophysiological mechanism and clinical presentation of its complications are numerous, ranging from self-limited disorders with a very good prognosis (Case 1) to severe ones with major sequelae (Case 2). Neurologists should get acquainted with these complications as they may be called upon to manage them.

Disclosure: Nothing to disclose

EP1198

Polio-like disease: A case report

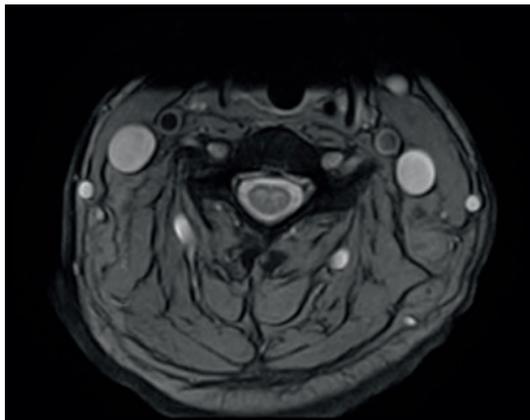
L.B. Lara Lezama, L. Redondo Robles, B. Clavera de la Gándara, A. Álvarez Noval, J. Hernández Rodríguez, E. Solanas Letosa, G. Rodrigo Stevens, N. González Nafria, L. Hernández Echebarría, J. Tejada Garcia, J.F. Fernández López

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Background and aims: Since the introduction of the vaccination against poliovirus, poliomyelitis has become a disease virtually eradicated in developed countries. In 2016, the National Spanish Institute of Epidemiology reported 60 cases of pediatric patients with acute flaccid paralysis or rhombencephalitis, identifying in 5 of them non-polio enteroviruses.

Methods: 63-year-old male patient, consulted with acute onset of occipital headache, fever and general discomfort. Successively, dysphonia, dysphagia and cervical weakness were added. Neurological exploration revealed bilateral ptosis, dysphonia, severe weakness for cervical flexoextension, generalized hypoactive myotatic reflexes, flexor plantar reflexes and normal sensory examination. He presented a rapid progression to severe asymmetric proximal weakness of superior limbs with respiratory distress secondary to bilateral phrenic paralysis requiring admission in the intensive care unit.

Results: Cerebrospinal fluid (CSF) revealed 43 leucocytes/mm³ (68% mononuclear), proteins 85 mg/dl and normal glucose. Gram's stain, CSF culture and neurotropic virus serologies were negative. Polymerase chain reaction for enterovirus in CSF, nasopharyngeal aspiration and feces were negative. Successive electromyographies demonstrated acute denervation in upper extremities. Cerebral and spinal magnetic resonance identified non-enhancing hyperintense lesions in T2 sequences of the anterior horn of cervical (figure A and B), dorsal and lumbar spine. The patient was treated with intravenous methylprednisolone and immunoglobulins with partial recovery of the symptoms.



Magnetic resonance. T2 sequences. Non-enhancing hyperintense lesions in the anterior horn of cervical spine in axial (Figure A).



Magnetic resonance. T2 sequences. Non-enhancing hyperintense lesions in the anterior horn of cervical spine in sagittal (Figure B).

Conclusion: This is a case report of a patient with polio-like disease. Sometimes it is not possible to identify the etiological agent. Nevertheless, it is an entity to remember in the differential diagnosis of acute flaccid paralysis even in adult patients.

Disclosure: Nothing to disclose

EP1199

The effect of NeuroGel™ with neural crest stem cells implantation on motor function recovery after experimental spinal cord injury

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Background and aims: To examine NeuroGel™ with xenogenic neural crest stem cells (NCSC) implantation on rat's hind limb motor function recovery after experimental spinal cord injury.

Methods: Animals: outbred albino rats. Experimental groups: 1— spinal cord injury only (n=16); 2 — spinal cord injury +immediate homotopical transplantation of NeuroGel™ (n=20); 3 —spinal cord injury+analogous transplantation of NeuroGel™ in association with adult mouse NCSC (n=12). Group 3 consisted of 12 animals, respectively, —subgroups 3m and 3f. Model of injury — left-side spinal cord hemisection at T11; duration of observation —28 weeks; ipsilateral hindlimb function indicator (IHL FI) determination — the BBB scale.

Results: Significant differences between the group 2 and group 1 IHLFI noted during period of 2th–28th week ($p<0.001$), between IHL FI of the group 1 and group 3 — during the whole observation period ($p\leq 0.02$). The maximum prevalence of group 3 IHL I over the group 2 IHLFI pointed at 24thweek ($p=0.055$). Significantly ($p<0.05$) difference between IHL FI of the subgroup 3m and group 2 was found at the 5th–16th week, between IHL FI of the subgroup 3m and group 3f — during period of the 1st–6th week. Significant difference between the subgroup 3f and group 2 IHL FI was not observed, the maximum value of its difference was found at the 3rd–4thweek.

Conclusion: NCSC xenotransplantation generally changes the function recovery dynamics, conditioned a trend towards potentiation of the NeuroGel™ positive effect on the course of the spinal cord injury; efficiency of this influence significantly depends on the sex of recipient organism.

Disclosure: Nothing to disclose

EP1200

Soft surfaces provide different effects on walking characteristics spatiotemporal gait modification of ambulatory patients with spinal cord injury who walked with or without a device

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Background and aims: Soft surfaces offer unstable supporting area that may alter walking characteristics of patients with impaired walking ability such as those with spinal cord injury (SCI).Therefore, this study aim to investigate spatiotemporal gait characteristics of 15 ambulatory participants with SCI who walked with (n=8) or without (n=7) a walking device while walking on hard and 3inches thickness soft surfaces.

Methods: The participants were assessed for their demographics, SCI characteristics, and spatiotemporal gait parameters while walking over a 10-m walkway of hard and soft surfaces. Findings of each surface were compared using the paired simple t-test.

Results: Walking on a soft surface attributed obvious effects on step length and cadence of participants who did not use a walking device ($p<0.05$). However, for those who used a walking device, walking on soft surface significantly affected only in walking cadence ($p<0.05$).

Conclusion: The different effects of soft surfaces on walking characteristics of those who walked with or without a walking device may suggest the contribution of upper limb functions when they encountered a challenging task as that seen in those who used a walking device. The findings may suggest the risk of falls for these individuals when they participate in a different surface from that commonly used in rehabilitation settings. Thus the incorporation of soft surfaces during walking training may promote rehabilitation outcomes for the patients.

Disclosure: This study was supported by funding support from the Research and Researchers for Industries or RRI and the Improvement of physical performance and Quality of life Research groups, Khon Kaen University, Thailand.

EP1201

Myelopathy chameleons - they're out there!

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Background and aims: Cervical spondylotic myelopathy (CSM) is a common, underdiagnosed and potentially debilitating disorder, with significant clinical heterogeneity. Despite its prevalence, delayed or misdiagnosis of CSM is still frequent nowadays.

Results: Case 1: A 61-year-old female was observed for a right foot drop, with numbness, and was given the diagnosis of diabetic neuropathy. She presented to us one year later having developed a left foot drop plus weakness and numbness in both hands. Neurological examination revealed hyperreflexic quadriparesis with right side predominance, bilateral Hoffmann and Babinski signs, hypoesthesia and hypopallesthesia of hands and lower limbs, with sensory level at D6. Spinal MRI showed severe spinal stenosis with myelopathy at C5-C6 level. The patient underwent cervical laminectomy and, at one-year follow-up, exhibited partial recovery of strength.

Case 2: A 76-year-old male presented with a one-year history of progressive stepwise left limbs weakness, at first confined to the lower limb, and hence attributed to lumbar radiculopathy. Neurological examination uncovered bilateral upper limbs and torso fasciculations and hyperreflexic left hemiparesis with Babinski sign. Cervical MRI revealed spondylotic myelopathy at C3-C6 levels. Six months after cervical laminectomy, there was only a mild left crural paresis remaining.

Conclusion: These two patients' atypical presentation of CSM incited a lengthy diagnosis and late referral to surgery. Given the lack of pathognomonic symptoms, identification of CSM requires a high index of suspicion. It is imperative to keep improving the awareness of the disorder, especially regarding unusual presentations, since early diagnosis and treatment limits disease progression and prevents irreversible neurological impairment.

Disclosure: Nothing to disclose

EP1202

Heterotopic ossification and spinal cord compression: Long-term follow-ups of a patient with implant in the cervical spine after incomplete spinal cord injury

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Background and aims: This case study examines long-term biomechanical changes caused by a total disc replacement in a 34-year-old female patient after traumatic incomplete spinal cord injury C5/C6 and cervical myelopathy, AIS D sub C5.

Methods: 10-year follow-ups. First MRI was done prior to surgery. Clinical, radiological (X-rays, CT, MRI, myelography of the spine), electrophysiological examinations (Somatosensory and Motor Evoked Potentials SSEPs/MEPs, NLG, EMG) were acquired yearly because of fluctuating neurological symptoms.

Results: After implant the patient showed slight problems with bladder function and hypoesthesia in the complete left leg. 9 months later intermittent pain in the cervical spine and a worsening of bladder function occurred. CT scans, X-rays and myelography proved an osteophyte level C5/6. Slight protrusions within presurgical MRI level C4/5, C6/7 became more prominent. Heterotopic ossification in the level of implant and disc protrusions were progressive and finally diagnosed as disc bulging in 7-year follow-up report for MRI. SSEPs were normal, MEPs showed a slight increase of the resting motor threshold of the left leg. NLG/EMG was regular. The 10-year follow-up report showed further aggravation of the clinical parameters.

Conclusion: Heterotopic ossification in the level of implant and disc herniation in the adjacent spine segments were detected at least 9 months post implantation with progression in the further time course. Altered biomechanical stress due to the implant could be responsible to these secondary changes beyond age-related degenerative alterations. Long-term biomechanical effects of implantation should be taken into consideration and should lead to further research implant improvement with regard to material and biomechanics.

Disclosure: Nothing to disclose

EP1203

Spinal arteriovenous fistulas: Critical issues in differential diagnosis and therapy

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Background and aims: Spinal arteriovenous fistula (SAVF) is a rare cause of myelopathy, frequently misdiagnosed as myelitis. Our aim is to describe a case of SAVF, summarizing the main features of this pathology to help future early diagnosis.

Methods: A 57-year-old male was hospitalized for paresthesia and stiffness in both legs: the symptoms started a year before, after he had undergone bone marrow transplantation for an acute myeloid leukemia, successfully treated with fludarabine and busulfan. Over the past two months the symptoms worsened quickly. Neurological examination showed hypopallesthesia, hypertonia and hyperreflexia in both legs, Babinski sign on the left and hypoaesthesia under D12 level.

Results: An EMG showed a mild axonopathy in both legs. A longitudinally extensive dorsal myelopathy from D7 to D12 segments was detected at a spinal MRI scan. We first postulated an inflammatory disease, supported by mild increase of CSF proteins. A steroid therapy was started, but after two days the symptoms worsened, resulting in severe gait disturbances. At this point the hypothesis of SAVF was formulated and confirmed by MRA scan, which evidenced a spinal venous congestion, and eventually by a spinal DSA. We promptly started a mannitol therapy to reduce the edema with benefit, while the patient was waiting for surgical intervention.

Conclusion: Although SAVF is a rare condition, it should be considered in the differential diagnosis of longitudinally extensive myelopathies. This is much more worthy as steroid therapy may result in symptoms worsening. Spine MRA scan should be performed in the setting of longitudinally extensive myelopathies.

Disclosure: Nothing to disclose

EP1204

Spinal cord ischemia syndrome due to anterior spinal artery occlusion: A case report

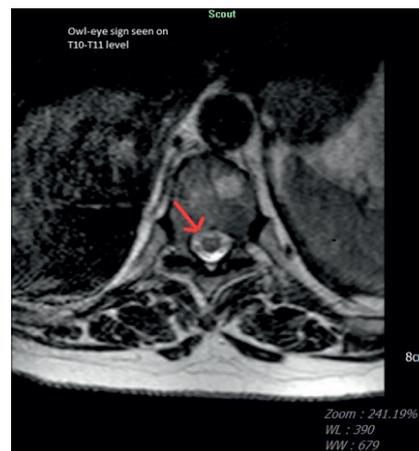
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Background and aims: Spinal cord ischemia is a rare disease compared to cerebral ischemia because of the rich anastomatic vessels of the spinal cord. Acute spinal cord ischemia syndrome represents <1% of all strokes. Diagnosing the occlusive vascular lesions of the spinal cord is challenging and there is a need to clear the aetiology.

Methods: 60-year-old female presented with severe pain starting from the right hip extending to the right leg spreading to the left leg and abdomen. Her medical history revealed diabetes, hypertension and lumbar disc hernia. At the admission she had flaccid paraplegia on both limbs. Analgesia was present under T10 level, plantar responses were indifferent

Results: The cranial, cervical, thoracic and lumbar MRI showed no findings of a mass or myelitis. In the thoracic segments increased T2 signals were seen on the anterior spinal cord from T5 to conus medullaris. Thoracic disc protrusion was seen on T3-4 level. The patient was diagnosed with spinal cord ischemia syndrome and was treated with acetylsalicylic acid and LMWH.



Owl-eye sign seen on T10-T11 level



Thoracic disc hernia seen on T3-T4 level and increased T2 signals seen below T5 level

Conclusion: Spinal cord infarcts are usually present with acute radicular pain, radiating caudally, combined with paraplegia, paresthesia and sphincter dysfunction. The aetiology includes atherosclerotic and aortic pathologies, trauma or emboli. Fibrocartilaginous emboli resulting from a herniated disc is also an important cause of the spinal infarct which is seen in our case. Gold standard diagnostic tool is the spinal MRI. Spinal MRI is also used to exclude other pathologies of the spinal cord. Increased T2 signals in the cord, owl-eye sign on axial sections is typical.

Disclosure: Nothing to disclose

EP1205

Catastrophic arachnoiditis following posterior fossa aneurysmal subarachnoid haemorrhage.

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Background and aims: Arachnoiditis is a rare complication of subarachnoid haemorrhage (SAH) with less than 30 cases reported. It commonly presents following a posterior fossa aneurysm, with haematomyelia being the proposed trigger of the inflammatory response.

Methods: We present a case and review the literature.

Results: A 55-year-old right-handed carpenter, presented with three week history of sudden onset band-like thoracic chest pain, followed by progressive numbness and weakness of both legs and micturition difficulty. Three months prior, he had a spontaneous SAH secondary to two posterior inferior cerebellar artery aneurysms; these were clipped and he made a complete recovery. Examination showed myelopathy with a T9 sensory level and urgent MRI showed extensive arachnoiditis of the cervical, thoracic and lumbar spine with cauda equina compression. He was transferred to a neurosurgical unit and had an attempted laminectomy and drain insertion; weakness worsened significantly post-operatively. Two subsequent courses of IV methylprednisolone had no effect and he was left with spastic paraplegia, incontinence and T6 sensory level.

Conclusion: Post-SAH arachnoiditis is rare, with no consistent approach to treatment and variable outcomes reported. Most cases, as in our patients, follow posterior fossa aneurysms. Given the significant time delay following the initial SAH, this important diagnosis can be missed in the early stages. Unfortunately in our patient, neither surgery or immunomodulatory treatment altered the disease course, however early intervention may lead to better outcomes.

Disclosure: Nothing to disclose

Peripheral nerve disorders 1

EP1206

Optimal treatment in CIDP (OPTIC protocol): Combined intravenous immunoglobulin and methylprednisolone as induction treatment

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Background and aims: Intravenous immunoglobulin (IVIg) and pulsed corticosteroids are both efficacious first choice treatments in CIDP. Each has its own benefits. IVIg has a fast mode of action usually leading to improvement within 6 weeks of treatment. Alternatively, corticosteroids can lead to long-term remission, defined as sustained improvement after stopping treatment. As fast improvement and long-term remissions can both be regarded as equally important, we hypothesized that combining IVIg and pulsed corticosteroids will lead to a higher rate of improvement, faster improvement and more frequent long-term remission in CIDP compared to treatment with IVIg or corticosteroids alone.

Methods: We started a prospective open-label uncontrolled feasibility study with a convenience sample of 20 probable or definite CIDP patients according to the EFNS/PNS criteria. Patients are treated with 3-weekly pulses of IVIg (2g/kg in first week followed by 1g/kg) and 1000 mg intravenous methylprednisolone during an 18-week period. Primary outcome is the number of patients in remission at 1 year after start of treatment.

Results: So far, the OPTIC protocol was initiated in eighteen patients. Thirteen completed treatment period, in two treatment was adjusted because of adverse events (toxicoderma, diverticulitis) and two patients are still being treated. One patient discontinued treatment because of a myocardial infarction. Fourteen of sixteen patients improved to a level that further treatment was regarded unnecessary. During a median follow-up of eight months off treatment, eight patients are currently in remission, five experienced a relapse and one died from a cause unrelated to CIDP or treatment.

Conclusion: Results expected in 2018

Disclosure: Nothing to disclose

EP1207

Paucisymptomatic sensory neuropathy associated with familiar chronic cough and gastroesophageal reflux

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Background and aims: Sensory-motor hereditary neuropathies are a heterogeneous group of neurodegenerative disorders defined by progressive neuropathy. Those with prominent sensory features and autosomal dominant inheritance are classified as Hereditary Sensory Neuropathies I (HSNI). In 2002, Springs described Hereditary Sensory Neuropathies I (HSNIB), characterized by adult onset paucisymptomatic sensory axonal neuropathy, chronic cough and gastroesophageal reflux. Non responsible gene has been identified but linkage to chromosome 3p22-p24 has been notified. We present 3 cases from the same family with hereditary sensory neuropathy with cough and gastroesophageal reflux.

Methods: We identify 3 brothers (2 females, 1 male), aged between 43 and 52 years. All of them refer chronic cough of unexplained etiology beginning in young-adult life and at least one of them symptoms of gastroesophageal reflux without response to proton-pump inhibitors. Only the eldest presents paresthesias and painful cramps in lower extremities.

Results: Electroneurogram demonstrates the existence of axonal sensory neuropathy of variable severity in the 3 siblings. A molecular study is performed after obtaining DNA from peripheral blood samples. The technique involves the expansion of 4 microsatellites located on chromosome 3p (D3S2403, D3S2336, D3S2466 and D3S1266). The three patients share a haplotype of 3 of these markers located in the 3p22-p24 region.

Conclusion: We consider of great interest to contribute 3 new cases that share haplotype of 3 of the 4 markers that previously had been associated with HSNIB. Symptoms derived from sensory neuropathy are mild and appear later than cough or gastroesophageal reflux. Therefore it could be an underdiagnosed entity.

Disclosure: Nothing to disclose

EP1208

Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP) associated with peritoneal dialysis

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Background and aims: A rapidly progressive demyelinating polyneuropathy has previously been described in the context of severe renal failure in individuals undergoing continuous ambulatory peritoneal dialysis (CAPD). However, literature searches identified only three case reports demonstrating a clear temporal relationship between commencing CAPD and rapid onset of severe demyelinating polyneuropathy, and none following haemodialysis. We describe another case of polyneuropathy following CAPD that is also supported by ultrasound imaging.

Methods: Case report and literature review. Literature search using Ovid and Pubmed databases.

Results: A 28-year-old male became anuric with end stage renal failure (ESRF) due to staghorn calculi. He was commenced on CAPD but developed severe sensory loss in hands and feet within one month of starting treatment. This was followed by severe proximal and distal weakness affecting all limbs. He became unable to walk or care for himself. Neurophysiology showed absent sensory responses and slowing of motor responses. Cerebrospinal fluid was acellular with raised protein. Ultrasound demonstrated diffuse swelling of the median nerve and nerve roots (Figure.1). To the authors' knowledge, this is the first description of nerve ultrasound findings in such a patient. There was improvement of proximal but not distal weakness, and improved disability following intravenous methylprednisolone, five cycles of intravenous immunoglobulin and switching to haemodialysis.



Figure. 1: An ultrasound image showing swelling around the C5/6 nerve root.

Conclusion: We describe a further case of a severe demyelinating polyneuropathy associated with CAPD, with ultrasound imaging. This may represent a subtype of chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). We postulate an immune mediated mechanism triggered by a peritoneal reaction.

Disclosure: Nothing to disclose

EP1209

Novel approaches to the treatment of polyneuropathy induced by diabetes type 1

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Background and aims: The aim of the study was to investigate the biomechanical characteristics of skeletal muscle contraction rats with diabetes and exposure to the drug "Cocarnit."

Methods: The study were conducted on 30 white nonlinear laboratory rats, which were divided into 3 groups of 10 animals each. Group 1 rats were used as control. In rats of the second and third groups were induced type I diabetes by administration of streptozotocin (STZ) (65mg/kg, i/p). Rats in group 2 was administered saline, and rats 3rd group – Cocarnit (1mg/kg, i/p, complex of nicotinamide, thiamine pyrophosphate, cyanocobalamin and adenosintriphosphate sodium) (company World Medicine) during 9 days. To determine the basic parameters of the dynamics of skeletal muscle contraction in rats was performed modulated stimulation of isolated nerve bundles on anesthetized rats with simultaneous detection of force reduction tibia muscle with discrete control changes its length under constant external load.

Results: It was established that diabetic neuropathy results in suppression of skeletal muscle contraction dynamic parameters due to time delay realization of muscle efferent stimulation; increasing delay realization of efferent stimulation with increasing time of active muscle; suppression of speed-power parameters muscle contractions within the studied time range; violation of the time correlation between the level of efferent activity flowing to the muscles and their realization in muscle system. Cocarnit restored biomechanical characteristics skeletal muscle of rats with diabetes.

Conclusion: Obtained results indicates that the consequence of diabetic neuropathy is nerve conduction abuse that cause accurate positional movements violations and Cocarnit restored investigated biomechanical parameters

Disclosure: Nothing to disclose

EP1210

Giant axonal neuropathy diagnosed with Next-generation sequencing technology

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Background and aims: Next-generation sequencing (NGS) or massively parallel sequencing detects the precise order of nucleotides within a DNA molecule. NGS is more effective than traditional sequencing methods, such as Sanger sequencing, when several genes are involved. Targeted NGS is starting to be used in diagnostics for disorders caused by several genes. About 100 genes may cause hereditary neuropathies. Charcot-Marie-Tooth disease (CMT) is the most frequent hereditary neuropathy with a prevalence of 40-80 per 100,000 in Norway. Giant Axonal neuropathy is a rare form of hereditary neuropathy with autosomal recessive inheritance caused by mutations in the gigaxonin gene (GAN).

Methods: A 7-year-old girl with progressive neuropathic features and corkscrew curly hair was investigated. Nerve conduction velocities were in the axonal range. She was previously diagnosed as CMT type 2.

Results: NGS revealed compound heterozygous GAN mutations. Some of her clinical features were also indicative of the diagnosis.

Conclusion: Giant axonal neuropathy is progressive and may cause severe functional deficits, later symptomatology from the central nervous system and reduced life expectancy. One of the GAN mutations was novel.

Disclosure: Nothing to disclose

EP1211

Foot drop of tumoral origin: An unusual etiology

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Background and aims: Foot drop is frequently due to peroneal nerve compression. The nerve is vulnerable to external forces, including persistent postures, because its superficial position at the neck of the fibula. We present two clinical cases of foot drop in which the study revealed a tumoral cause.

Methods: Patient 1: A 55-year-old woman presented with repeated falls, distal hypoesthesia in her lower left limb and progressive left foot drop. She had impaired foot dorsiflexion, weakened plantar flexion, abolition of the ankle reflex, and hypoesthesia in the lateral leg, dorsum of the foot and heel.

Patient 2: A 31-year-old woman presented with a foot drop that had evolved over 3 months. She had severe impairment of left foot dorsiflexion and toe extension, gastrocnemius and peroneal atrophy, and a diminished ankle reflex.

Results: Patient 1: An electroneurogram (ENG) revealed damage of both left common peroneal and posterior tibialis nerves. Magnetic resonance imaging (MRI) of popliteal fossa showed multiple adenopathies suggestive of a lymphoproliferative disorder with extrinsic nerve compression. The final diagnosis was a non-Hodgkin lymphoma.

Patient 2: The ENG revealed damage of the left common peroneal nerve. MRI of the lower thigh showed an area of thickening of peroneal nerve, which was later revealed to be a neurofibroma.

Conclusion: Despite usually having a benign cause, foot drop with atypical features should prompt an adequate work-up. Attention should be paid to findings suggesting associated deficits of other nerves such as decreased ankle jerk. Our cases highlight that tumours should be considered among the possible etiologies.

Disclosure: Nothing to disclose

EP1212

Preserved muscle strength but deterioration in aerobic capacity after discontinuation of regular exercise in patients with chronic inflammatory demyelinating polyneuropathy

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Background and aims: In a previous study we demonstrated that in patients with chronic inflammatory demyelinating polyneuropathy (CIDP), aerobic exercise led to a significant increase in aerobic capacity of 11% and following unilateral resistance exercise muscle strength increased significantly by 14% in trained extremities and 4% in non-trained extremities. In this one-year follow-up study we evaluated whether muscle strength and aerobic capacity was preserved despite discontinued formalized exercise.

Methods: In our previous study, fifteen CIDP patients performed 12 weeks of aerobic exercise on ergometer bike and 12 weeks of unilateral resistance exercise of muscles at the knee and elbow. After participation no scheduled training was initiated. We performed a one-year follow-up test with measurement of isokinetic muscle strength by dynamometry and evaluation of aerobic capacity by determining maximal oxygen consumption velocity.

Results: Ten out of fifteen patients from the initial study participated. Combined isokinetic muscle strength (cIKS) had changed insignificantly with $-3.4 \pm 17.6\%$ and $-2.9 \pm 14.7\%$ on the trained and non-trained side, respectively. Aerobic capacity had decreased by $14.8 \pm 9.5\%$ ($p=0.002$). Compared to baseline before exercise cIKS had increased $15.6 \pm 20.5\%$ ($p=0.04$) on the trained side whereas on the non-trained side the difference was only $3.0 \pm 12.9\%$ (ns). Aerobic capacity had changed only $1.6 \pm 13.8\%$ (ns). During the one-year follow-up only two patients had performed regular aerobic exercise, and one patient had performed regular resistance training.

Conclusion: Muscle strength was preserved one year after resistance training despite discontinuation of training whereas aerobic capacity had fallen to a level comparable prior to training.

Disclosure: Nothing to disclose

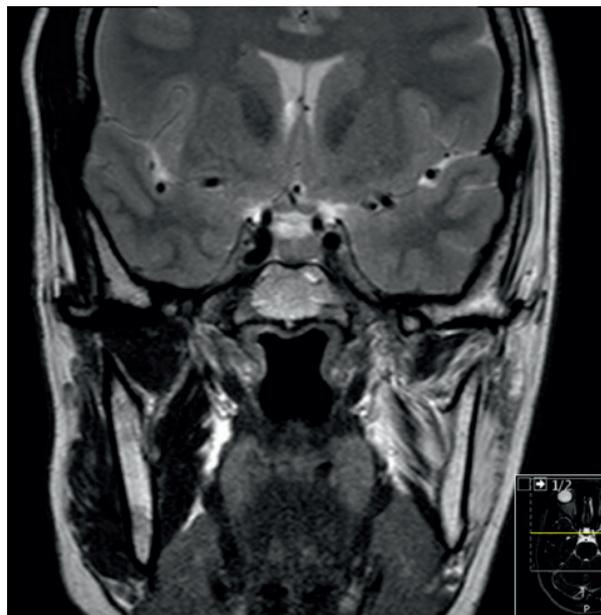
EP1213

A rare cause of facial asymmetry

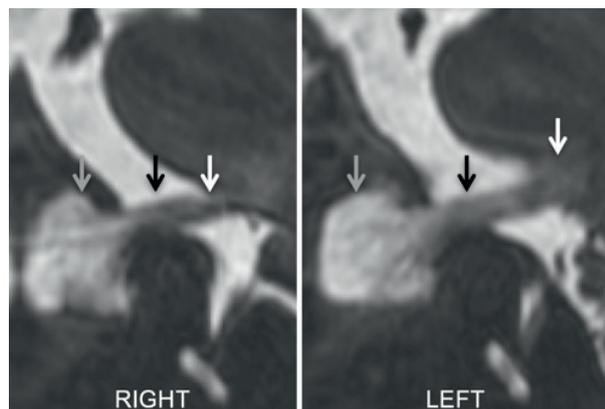
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Background and aims: We report a patient presenting with facial asymmetry due to isolated unilateral trigeminal motor neuropathy.

Results: A 40-year-old woman presented with progressive facial asymmetry, left hemifacial numbness and pain for the last month. She denied past history of head or facial trauma, dental procedures, diabetes herpes-zoster or other infections, as well as systemic symptoms. On neurological examination it was disclosed left temporal and masseter muscle atrophy, left deviation of the mandible on opening of the mouth, and mild poorly-defined left hemifacial hypoesthesia. Electrophysiological study confirmed the diagnosis of pure motor trigeminal neuropathy, with chronic neurogenic potentials in the atrophic muscles. Trigeminal sensory fibers were normal on blink reflex and facial laser-evoked potential. Facial and cranial MRI revealed atrophy and fatty infiltration on left masticator muscles (figure 1) and regular thickening of the affected fifth cranial nerve at its origin in the anterolateral surface of the pons, extending to cisternal portion and Meckel's cave (figure 2), which suggested an inflammatory lesion. Blood and cerebrospinal fluid studies were negative for autoimmune and infectious diseases. Clinical picture remained stable over 9 months of follow-up.



Facial MRI coronal. Fat infiltration on left masticatory muscles



Cranial MRI, T2 3D DRIVE HR, reformatted images along the trigeminal nerves. Thickening and hyperintense signal on apparent origin (white arrows), cisternal segment (black arrows) and Meckel's cavum (gray arrows) of the fifth cranial nerve.

Conclusion: Trigeminal neuropathy is usually characterized by motor and sensory involvement. Reviewing the literature we found that 16 similar cases have been reported. As described in some other patients, sensory symptoms were referred in spite of isolate motor involvement on neurophysiology investigation. There is a wide array of possible etiologies for this neuropathy, however in most of the cases, no apparent cause is found.

Disclosure: Nothing to disclose

EP1214

Bilateral carpal tunnel syndrome as an adverse effect of Pembrolizumab

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Background and aims: Pembrolizumab is a monoclonal antibody approved for treatment of metastatic melanoma and non-small cell lung cancer. We report a case of acute bilateral carpal tunnel syndrome as a possible adverse effect to Pembrolizumab.

Results: A 77-year-old man presented with progressive paresthesia and numbness in fingers and hands for the last month. Five months before he had started treatment with Pembrolizumab 2mg/kg IV every three weeks for metastatic melanoma. He denied similar symptoms on the past. He rejected recent repetitive manual activity, distal edema or arthritis symptoms. On neurological examination it was disclosed bilateral positive Phalen sign and hypoesthesia in median nerve territory. Nerve conduction studies confirmed severe bilateral carpal tunnel syndrome, without signs of peripheral neuropathy. Bilateral carpal infiltration with betamethasone dipropionate and levobupivacaine was performed, with major symptomatic and electrophysiological improvement over the following week. Pembrolizumab treatment was continued and three months later he remains clinically well, with continued neurophysiological recovery.

Conclusion: This is the first report of bilateral carpal tunnel as an adverse reaction to Pembrolizumab. One of the possible mechanisms could be a bilateral tenosynovitis of the wrist, as this condition has been reported as an uncommon adverse reaction to this drug. In our patient we found a segmental demyelization, in a local prone to nerve compression, as the most probable explanation.

Disclosure: Nothing to disclose

EP1215

20-year follow-up of Lewis-Sumner Syndrome with several cranial nerve palsies

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Background and aims: To describe a patient with Lewis-Sumner Syndrome (LSS) characterized by a long follow-up, a relapsing and benign course and atypical cranial palsies.

Methods: A 49-year-old male consulted because of sudden diplopia and right upper limb weakness the previous 6 months acutely worsened. On physical examination he had an incomplete third cranial nerve palsy of the on right side, a subtle proximal weakness and hypoesthesia in that upper limb, the rest of the neurologic exam being normal.

Results: All of the complementary exams and laboratory tests were normal (blood cell count, routine biochemistry, immunology including autoantibodies such as anti-GQ1b, GM1, infectious serology and cerebrospinal fluid). The thorax film revealed a new right diaphragmatic elevation that resolved with time. The electrophysiological study showed persistent multifocal conduction block. The patient had a spontaneous complete recovery after two weeks. During his evolution he suffered six relapses coinciding with fever and different infectious diseases.

In some relapses he showed new cranial nerves involvement: right reversible diaphragmatic elevation, right hypoglossal palsy, right facial palsy and right trigeminal involvement. After all episodes the recovery was complete.



Conclusion: LSS is an asymmetric sensorimotor neuropathy, considered as a variant of chronic inflammatory demyelinating polyradiculopathy. Clinically, it is characterized by predominant upper limb impairment and electrophysiologically it shows a persistent multifocal conduction block. We present a patient with 20 years follow-up LSS characterized by multiple cranial nerve involvement, among which, X and XII nerve palsies have not been described in the literature yet.

Disclosure: Nothing to disclose

EP1216

Subacute polyradiculoneuropathy: Is vitamin deficiency a cause? About 3 cases

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Background and aims: Peripheral neuropathy due to vitamin deficiency may have a misleading clinical presentation and mimic Guillain-Barré Syndrome. We present 3 cases of rapid onset peripheral neuropathies with potential vitamin deficiency context.

Methods: We identified 3 patients aged from 28 to 31 years old presenting with subacute 4 limbs sensorimotor peripheral neuropathy with potential vitamin deficiency context : a woman who had gastric by-pass with post-surgery vomiting and 65kg weight loss, a woman with depression, anorexia and 25kg weight loss, and a man with alcoholism, recent vomiting and 3kg weight loss.

Results: Electroneuromyography showed 4 limbs sensorimotor non length dependent neuropathy, with demyelinating features without official criteria. Cerebrospinal fluid study was normal. Immunologic and infectious study were negative. We found B1 and B9 vitamins deficiency for 2 of 3 cases, which was considered as a cause with clinical and electrophysiological slow improvement after supplementation. For the third case, only B9 vitamin deficiency was found and we considered it as an acute demyelinating polyneuropathy complicating an old axonal polyneuropathy. Slow improvement was observed after intravenous immunoglobulins treatment. These 3 cases have a common history of potential vitamin deficiency. We discussed both inflammatory and carential etiologies but neither electroneuromyography nor cerebrospinal fluid study brought a clear answer.

Conclusion: B1 vitamin deficiency is a cause of rapid onset neuropathy needing quick treatment. It is important to know when to think about it but also search for other diagnosis with specific treatment.

Disclosure: Nothing to disclose.

EP1217

Predicting factors of clinical outcome in chronic inflammatory demyelinating polyneuropathy

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Background and aims: Chronic inflammatory demyelinating polyneuropathy (CIDP) represents a heterogeneous group of symmetric classical sensorimotor, pure motor, sensory ataxic and Lewis Sumner form. The aim was to examine relationship between different factors (gender, age at disease onset, course and severity of disease, CSF protein level, comorbidities and treatment procedure) and clinical outcome of different forms.

Methods: This retrospective study included 48 CIDP patients classified in 4 groups in relation to clinical form.

Results: The classical form had 39 patients, pure motor 5, Lewis Sumner 3 and one had sensory ataxic form. Majority of patients with classical form had relapse remitting course (69.7%), while 30.8% of patients had progressive course. Stable remission in this group was achieved in 61.5% cases, improvement in 30.8%, and in 7.7% of patients disease continued to progress. Logistic regression analysis showed that all risk factor included in the study are in correlation (positive or negative) with clinical outcome of classical form, but none of this correlation was statistically significant. Highest predictive value had disease severity ($r=-0.285$), treatment with IVIG ($r=0.27$) and CSF protein level ($r=-0.228$). Only one patient with motor form had progression after treatment onset, this was female patient with MGUS IgM, high CSF protein level, progressive course and most severe form of the disease.

Conclusion: Considering all risk factors through specific score based on predictive value of each factor, we can predict clinical outcome of classical form of CIDP with high statistical probability (88.5%).

Disclosure: Nothing to disclose

EP1218

Cancelled

EP1219

Descriptive study of an Algerian cohort of anti-ganglioside antibody neuropathies: Clinical, electrophysiological and immunological aspects

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Background and aims: Anti-ganglioside antibody (AGA) neuropathies are dysimmune, rare and heterogeneous neuropathies. These AGAs are attracting increasing diagnostic interest, especially since the emergence of the concept of "nodo-paranodopathies" To study the association between neuropathic syndromes and AGA in our patients and to analyze these results in the light of recent concepts.

Methods: A retrospective, descriptive monocentric study in the EHS Ait-Idir neurology department in collaboration with the immunology department of Pasteur Institute of Algeria. All patients had acute or chronic peripheral neuropathy, associated with, at least, one anti-ganglioside antibody.

Results: Ten patients were included. Multifocal motor neuropathy was the most frequent phenotype. The others phenotypes were pure axonal and motor forms of the Guillain-Barré syndrome, sensory ataxic neuropathy, an "overlap syndrome" between MMN and MADSAM and an ALS syndrome. The most frequent AGAs were anti-GM1 (80%) and anti-GD1b (70%). The most frequent association was anti-GM1 and anti-GD1b. An association between AGA and onco-neural antibodies was encountered in one patient. Our series includes characteristic forms, rarer and exceptional phenotypes. Undetectable antibody levels are the likely consequence of the involvement of different epitopes of nodal and paranodal region. The concept of "nodopathies" seems, at present, more appropriate to characterize these neuropathies and thus explain some "misleading" aspects.

Conclusion: This first study in Algeria highlights the phenotypic and immunological heterogeneity of neuropathies associated with AGA. The recent discovery of new antibodies targeting the antigens of the Ranvier node allows us to solve certain nosological difficulties.

Disclosure: Nothing to disclose

EP1220

An Italian multicenter database for the diagnosis and therapy of chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) and its variants

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Background and aims: Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is a chronic disabling disease that often improves with immune therapy. Several variants of CIDP were reported but their frequency and relation with CIDP remains unclear.

Methods: We implemented a web-based database to collect data from Italian patients with CIDP to determine the frequency and characteristic of these variants, the diagnostic criteria used, the possible evolution into typical CIDP, and their response to therapy.

Results: By January 2017 we included 319 patients with CIDP and variants (197 men, 122 women), aged 18-86 years (median 58) with a mean disease duration of 7.8 years (range 0.5-38). Based on clinical symptoms, CIDP was defined as typical in 88% and atypical in 12%. The diagnosis of CIDP fulfilled EFNS/PNS criteria in 81% of the patients while nerve conduction studies (NCS) were not diagnostic in 12% or available in 7%. CSF studies were diagnostic in 81% of the patients, nerve biopsy in 50% and imaging (US or NMR) in 56%. Two supplementary diagnostic criteria

including a relapsing course were present in 77% of patients with non diagnostic NCS (clinical CIDP). Improvement after one or more therapies was reported by 88% of treated patients with a positive response to IVIg in 74%, steroids in 51%, plasma exchange in 60% and immune suppressant in 36% without differences according to the fulfillment or not of EFNS/PNS diagnostic criteria.

Conclusion: This multicenter study provided useful information on the natural history, course, diagnosis and response to therapy in patients with CIDP and variants.

Disclosure: Kedrion Biopharma srl, Italy supported the cost of the Database. I received travel supports to attend Scientific Congress from CSL Switzerland and Kedrion Italy.

Sleep disorders 1

EP1221

Excessive daytime sleepiness as first symptom of adult Pompe's disease

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Background and aims: Pompe's disease is a clinically heterogeneous disorder of autosomal recessive inheritance caused by an alpha-glucosidase (acid maltase) deficiency. There are 3 age dependent phenotypes; a rapidly progressive infantile form that is usually fatal within the first year of life, and a slowly progressive juvenile and adult variant. Onset at adult age may vary from the second to sixth decade. Patients may present with a proximal myopathy of the limb girdle type and fatigue. In a later stage a considerable number of patients develop respiratory failure.

Methods: We report on a 61-year-old patient suffering from severe hypersomnolence since 6 months. During the night he would wake up several times. His wife noticed that his breathing was slow when asleep. He had no complaints of breathlessness or exercise intolerance

Results: A polysomnography showed frequent awakening, reduced baseline oxygen saturations, and periods of hypopnoea. Following a bronchoscopy he developed acute respiratory failure with severe hypercapnia. He needed mechanical ventilation for a month and was finally discharged from the hospital with nocturnal non-invasive ventilation. Extensive investigations were normal except for a mildly increased creatine kinase and an alpha-glucosidase deficiency. Pompe's disease was confirmed by DNA testing.

Conclusion: The diagnosis of adult onset alpha-glucosidase deficiency must be considered in patients with unexplained respiratory insufficiency. In our patient this was masked by excessive daytime sleepiness due to nocturnal hypoventilation.

Disclosure: Nothing to disclose

EP1222

Cancelled

EP1223

Sleep disturbances in systemic lupus erythematosus

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Background and aims: There are few studies that evaluate sleep disturbances and especially restless legs syndrome (RLS) in patients with systemic lupus erythematosus (SLE). The aims of this study were: 1.) to assess sleep disturbances in SLE 2.) to determine the prevalence of RLS 3.) to assess the clinical characteristics of RLS.

Methods: This is a case-control study of consecutive SLE patients. Assessment instruments included RLS Rating Scale, RLS Quality of Life Instrument, Pittsburg Sleep Quality Index, Epworth Sleepiness Scale, Hospital Anxiety and depression scale. For this study were recruited 26 consecutive patients with SLE and 26 patients in the control group.

Results: There were 23 females (88.46%) in the study group; the mean age was 52.35±10.76 years.

There were 9 patients that met RLS criteria (34.62%) in the study group and 2 patients (7.69%) in the control group (p<0.05). In the study group, the severity distribution of RLS was: mild - 1 case, moderate - 8 cases. In the control group there was one case with mild severity and one with moderate severity.

There was no excessive daytime sleepiness in any of the patients. However, 69.23% of the patients from the lupus group had the ESS score between 6-10, in comparison with 46.15% in the control group (p<0.05). Higher global PSQI scores were found in the study group.

Conclusion: This study confirmed the poorer sleep quality and higher prevalence of RLS in SLE patients.

Disclosure: Nothing to disclose

EP1224

A deficit in visual processing for both insomnia and obstructive sleep apnoea patients overcomes the effect of age

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Background and aims: To test perceptual processing in two sleep disorders, both a group of 23 insomnia disorder (ID) and a group of 19 obstructive sleep apnoea (OSA) patients were compared with 19 age-matched healthy controls (HC).

Methods: All the participants performed a visual search task in which they had to detect the presence/absence of a target (letter T) embedded in the 50% of trials into a set of distractors (letters Os, Xs, or Ls). Target's salience and distractors' numerosity were manipulated as independent variables, whereas accuracy and reaction times (RT) were recorded as dependent variables.

Results: Data generally confirmed the typical effects of visual search. Moreover, both ID and OSA patients reported significantly slower RT in comparison with HC. Interestingly, RT increased as expected with age in HC, whereas no correlation between age and RT was found for both ID and OSA patients.

Conclusion: Our results demonstrate the existence of a perceptual deficit occurring in both ID and OSA patients, consisting in a harder extraction of relevant visual information from noise. Finally, for both clinical groups the effect of age is hidden by the overwhelming effect of the disorder.

Disclosure: Nothing to disclose

EP1225

Impaired neurocognitive functions in patients with disorders of arousal

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Background and aims: Sleepwalking, sleep terrors, and confusional arousals are non-REM sleep parasomnias grouped under the category of disorders of arousal (DOA), resulting from incomplete arousals from slow wave sleep. Frequently DOA patients exhibited excessive daytime sleepiness leading to abnormal functioning during the day. Therefore, cognitive impairment might be observed in this subjects, but a comprehensive evaluation of this patients has not been performed. Accordingly, the aim of this study is to assess neurocognitive functions in DOA patients through a complete neuropsychological evaluation and to compare their performance with that of healthy controls.

Methods: 69 patients (62.3% male and 37.7% female, mean age 32.8 ± 14.1) with a diagnosis of DOA and 31 healthy controls matched for sex, age and education have been evaluated by means of a complete neuropsychological assessment battery.

Results: A significant impairment in Corsi block tapping test and Attentive Matrices (which respectively investigate visuo-spatial short term working memory and visual selective attention) was found in DOA patients in comparison to healthy controls. Additionally, significant correlations between percentage of N1 and Corsi block tapping performance ($r = -0.418$, $p < 0.022$), Attentive Matrices and number of awakenings ($r = -0.403$, $p = 0.027$) and sleep efficiency ($r = 0.374$, $p = 0.042$) were found.

Conclusion: A deficit in visuo-spatial working memory and in selective visual attention have been found in DOA patients. Moreover, our results suggest that sleep disruption, objectively assessed by PSG recordings, could explain the neuropsychological deficits.

Disclosure: Nothing to disclose

EP1226

Non-24-hour sleep-wake syndrome and melatonin secretion impairment in a patient with pineal cyst

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Background and aims: Non 24-hour sleep-wake syndrome is a circadian rhythm sleep disorder (CRSD) characterized by the inability to maintain a stable circadian rhythm that became progressive longer; this lead to impossibility to fall asleep at the desired time. The majority of cases remain idiopathic, while few studies demonstrated CRSD associated to hypothalamic lesions. The role of melatonin and pineal gland on sleep structure is still debating, since sleep disorder as well as lack of consequences on sleep structures has been reported after pinealectomy. We present the case of a 14-year-old girl with a wide pineal cyst and severe CRSD.

Methods: Prolonged polysomnographic recording, brain MRI, actigraphy, 24-hour melatonin serum curve and endo-rectal temperature measurement were collected.

Results: Brain MRI examination disclosed a 20mm pineal cyst without evidence of aqueductal or mesencephalic compression. The prolonged actigraphy demonstrated a free-running disorder with total inversion of sleep-wake cycle. Polysomnographic recording and endo-rectal temperature profile were within the normal. Melatonin curve showed blunted nocturnal peak (max 82ng/L, mean nighttime 68.5), normal total quantity of melatonin secretion (AUC 1118.5ng*h/L), and a shape suggesting higher morning levels of melatonin. Evening administration of melatonin up to 14 mg was able to restore the normal sleep-wake cycle.

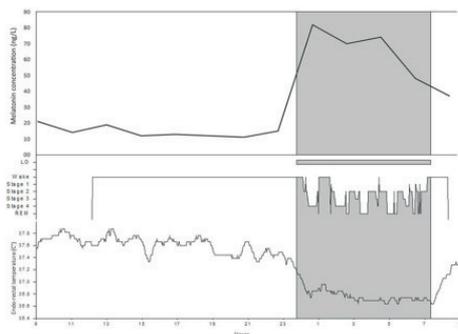


Figure 2: Melatonin curve plotting with hypnogram and rectal temperature. Note the Dim Light Melatonin Onset (DLMO) occurs 2 hours before sleep onset, while melatonin peak is anticipated and lower than normal subject. The graphical show dissociation between melatonin peak and lowest value of rectal temperature.

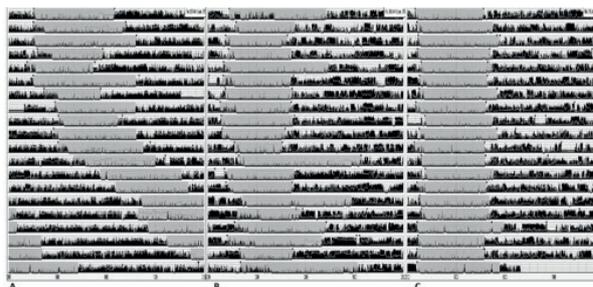


Figure 1: Homemade actigraphy. A: From the 6th day melatonin administration was discontinued. B: partial efficacy of 7 mg of melatonin at bedtime. C. Restoration of wake-sleep cycle after administration of 14 mg of melatonin.

Conclusion: The CRSD associated to melatonin secretion impairment were restored in our patient after melatonin administration. We speculate that the compression on the normal pineal parenchyma exerted by the cyst, may decelerate melatonin secretion with a slower return to basal concentration, leading to progressive sleep cycle advance.

Disclosure: Nothing to disclose

EP1227

Cancelled

EP1228

The Bern sleep database: A valid tool for clinical sleep research

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Background and aims: Multidisciplinary Bern Sleep-Wake-Centre was founded in 1982 and is a tertiary sleep-centre. Database is a useful tool in rare diseases for a better characterisation, evaluation, treatment, and research in the field. For over 25 years, patient data are collected in the Bern sleep database (BSD). In Bern, one of the main research and clinical areas always has been narcolepsy.

Aims: We aimed to set-up a new tool for sleep research including the development of predictive models to further assist clinicians in their diagnosis or treatment decisions.

Methods: BSD has been transferred into an application designed to support data capture and management for research studies. New BSD contains 13 forms/instruments with 720 potential items in total. Descriptive statistics has been executed.

Results: Patients: The total number of patients was 8543. Mean age was 49.0 years. Annual inclusion of new patients is continuously increasing since 2011 from 600/year to 1050/year in 2015.

Diagnosis: Diagnosis included sleep apnoea (N=5537), insomnia (N=476), narcolepsy (N=157) and excessive daytime sleepiness not otherwise specified (N=590). The annual number of new narcolepsy diagnosis maintained stable from 2000 to 2015 (10 to 15/year).

Tests: Data from 6500 polysomnographies, 1445 MSLT, 1823 “Bern sleep-wake-questionnaires”, and 2375 actigraphies are included. Data about narcolepsy and narcolepsy-borderland are currently under evaluation and will be presented.

Conclusion: The BSD is a unique database, including long-term data and will serve as a research tool for clinical sleep studies, validation of (new) diagnostic criteria or questionnaires, and the development of predictive models.

Disclosure: Nothing to disclose

Sunday, 25 June 2017

Ageing and dementia 2

EP2001

COMAJ (Early-Onset Alzheimer's disease cohort): Two-year follow-up

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Background and aims: Before 60, Early-Onset Alzheimer's disease (EOAD) is still the first cause of dementia. Atypical phenotypes are more frequent than in the elderly and disease course may be faster, and remains misunderstood. We aimed to describe clinical, neuropsychological, medical-social, autonomy and imaging courses of EOAD (onset before 60) patients on two-year follow-up.

Methods: All the patients of the prospective cohort COMAJ between the 01/06/09 and the 01/05/14 with probable or certain EOAD according to the NIA and IGW criteria were included, except those with autosomal dominant AD. Demographic data, vascular risk factors, APOE4 status, history, neuropsychological, medical-social, autonomy and MRI data were collected, according to a standardized protocol.

Results: 94 patients were included (women: 62%, mean age: 57.4±3.3 years, diagnostic delay 3.8 (2.2) years); 56% of the patients showed a typical amnesic phenotype, 44% were depressive, 62% were APOE4 carriers. APOE4 carriers were significantly more amnesic than the non-carriers (75.5% vs 36.3%, p=0.0007). Mean MMSE was 19.7 (5.7) at diagnosis, 14.1 (7.8) at inclusion and 9.8 (7.8) /30 on two-year follow-up. Mean Scheltens score was 1.8 at baseline and 2.5 two years later. Loss of autonomy was severe: only 8.5% (n=8) of the patients were working at baseline, none on follow-up. A daily help was required in 76% (n=71) of the patients at baseline, in 91% on two-year follow-up, with 26% living in institution at this time.

Conclusion: This large cohort provides information on the progression of the disease at early age, highlighting the severe and fast cognitive impairment.

Disclosure: Fund : Labex DistALZ

EP2002

Asymptomatic carotid stenosis might worsen cognitive functions in hypertensive patients

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Background and aims: Systolic arterial hypertension (SAH) in midlife is a risk factor for cognitive impairment (CI) but the relationship of asymptomatic carotid stenosis (ACS≥50%) to CI is still a matter of debate. The aim of this epidemiological study is to estimate the significance of ACS≥50% for CI in hypertensive and non-hypertensive persons without signs and symptoms of stroke or TIA.

Methods: A total of 500 volunteers, aged 50-79 years, were enrolled and followed-up for cognitive performance. CI has been defined as a score between 24 and 27 of MMSE. A battery of additional neuropsychological tests has also been conducted.

Results: Multiple logistic regression analysis has shown that ACS≥50% attributes to CI (OR=10.7; 95%CI: 3.36-34.14; p=0.0001) only in hypertensive patients with SAH but not in normotensives. Logistic regression analysis has revealed that the abnormal scores of neuropsychological tests (MMSE, DFS, DBS and VF) are significantly associated with ACS≥50% (OR 2.121; 95%CI: 1.048-4.292; p=0.036). The strongest relationship has been established between ACS≥50% and DBS (OR 10.818; 95%CI: 1.165-100.439; p=0.037). CI has presented as an executive dysfunction and decline of attention, verbal fluency and working memory.

Conclusion: ACS≥50% might be attributable to CI in patients with SAH. This suggests a complexity of a large and small artery dysfunction, caused by both atherosclerosis and hypertension, underlying the CI pathogenesis.

Disclosure: Nothing to disclose

EP2003

Alzheimer's disease environmental, biological and clinical risk factors in a Tunisian population

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Background and aims: Late-Onset Alzheimer's disease (LOAD) is a multifactorial idiopathic pathology caused by clinical, environmental and genetic factors. Hence its etiology is still unknown. We aimed to evaluate the main environmental, clinical and biological factors associated with this disease.

Methods: We enrolled 97 LOAD patients (diagnostic criteria: DSMIV and NINCDS-ADRD) and 284 controls. Data concerning clinical and biological parameters, life style and dietary habits were collected. Biostatistical analysis were conducted on SPSS.v20.0.

Results: After binary logistic regression, we noted that factors significantly associated with LOAD risk were hyperhomocysteinemia (OR=5.47; p=0.001), high total cholesterol levels (OR=6.78, p<0.001), high chlorine levels (p=0.034), decreased C-reactive protein and total thyroxine (T4) levels (p=0.042; p=0.046, respectively) hypocalcaemia (OR=2.6, p=0.038), hypovitaminosis-B12 (OR=5.4, p<0.001), hypovitaminosis-D (OR=5.48, p=0.001) smoking (OR=4.49; p=0.001), hypertension (OR=6.78, p=0.002), Diabetes (OR=4.89, p=0.003) and Chronic Kidney Diseases (OR=4.69, p=0.001). We also noted that high education level (OR=0.10, p=0.002), urban habitat (OR=0.30; p=0.032), currently or formerly active professional life (OR=0.20; p=0.016), consumption of fish (OR=0.21; p=0.012), olive oil (OR=0.18; p=0.015), curcuma (OR=0.10; p=0.026), coffee (OR=0.20; p=0.021) and black chocolate (OR=0.10; p=0.015) seem to decrease LOAD risk.

Conclusion: Our results support the hypothesis of cognitive reserve, which stipulates that the brain with cognitive reserve, ensured by an active social life and a high level of education, may protect against cognitive decline. It seems that a healthy life style and dietary habits mentioned above are recommended to prevent LOAD.

Disclosure: Nothing to disclose

EP2004

Antibodies against glial derived antigens in Alzheimer disease may reflect hippocampal demyelination and memory loss

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Background and aims: Alzheimer's disease (AD) is known to exhibit well characterized pathologies including the extracellular accumulation of amyloid plaques, intra-axonal presence of neurofibrillary tangles and glial hypertrophy. Nevertheless the nature of myelin pathology in AD has not been well studied. Recent studies on animal models of AD, revealed however focal demyelination within beta amyloid plaques in hippocampus. Thus we decided to assess humoral response against proteins of myelin sheath in AD, in hope to find an early biomarkers of memory loss and neuropathological process characteristic for the disease.

Methods: We assessed antibodies levels against proteins of myelin sheath: myelin oligodendrocyte glycoprotein (MOG), myelin basic protein (MBP), myelin-associated glycoprotein (MAG), proteolipoprotein (PLP) in sera of 26 AD patients and 26 healthy controls, using commercially available ELISA system (Mediagnost, Germany).

Results: In the AD patients subgroup significantly higher titers were observed for all types of assessed IgG autoantibodies compared to healthy control subjects (anti-MOG, anti-MAG, anti-MBP, anti-PLP). For IgM antibodies, among AD patients we observed higher titers for majority of investigated autoantibodies (p<0.05), with exclusion of anti-MAG IgM antibodies (p>0.05).

Conclusion: The study provides the evidence for the significantly increased production of autoantibodies against proteins of myelin sheath in AD. These results can be of importance in the light of emerging data from animal models of AD, indicating early demyelination of hippocampal region. Further studies on larger population are necessary to confirm whether these autoantibodies could serve as early biomarkers of AD in humans.

Disclosure: Nothing to disclose

EP2005

Apolipoprotein E ϵ 4 allele frequency in Korean patients with Parkinson's disease dementia

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Background and aims: It has been well known that the apolipoprotein E(ApoE) ϵ 4 allele is a strong risk factor in Alzheimer's disease and occurs at an increased frequency in dementia with amyloid pathology. However The clinical significance of the ApoE ϵ 4 allele in Parkinson's disease dementia(PDD) with synucleinopathy has been a subject of debate. PDD is one of the second most common subtypes of dementia in Korean population. The ApoE allele frequencies were evaluated in Korean patients with probable PDD diagnosed by the MDS task force criteria for the diagnosis of PDD in this study.

Methods: Forty patients (20 PDD and 20 age matched healthy controls) participated in the study. The ApoE genotype was determined by the polymerase chain reaction (PCR) and allele specific hybridization using the ApoE typing test kit. (DNA extraction: Wizard Genomic DNA purification kit (Promega), Polymerase chain reaction : Commercial INNO-LiPA (Line Probe Assay) ApoE test kit)

Results: The ApoE ϵ 4 allele frequency in the PDD group was 35% and was significantly higher than those of normal controls (15%) ($p < 0.05$). The ApoE ϵ 4 carrier frequency in the PDD group was 60%, and also significantly higher than those of normal controls (30%) ($p < 0.05$). The ApoE ϵ 3 allele was the most frequent genotype in Korean population generally in this study.

Conclusion: These results that the elevated ApoE ϵ 4 frequency in the PDD with synucleinopathy in which the overall brain neuritic plaque burden was low, indicates that ApoE ϵ 4 might contribute to neurodegeneration through mechanisms unrelated to amyloid processing

Disclosure: Nothing to disclose

EP2006

Cancelled

EP2007

SORL1 mutations in familial Alzheimer's disease

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Background and aims: The sortilin-related receptor 1 gene (SORL1) encodes a protein involved in the trafficking of amyloid precursor protein. Some SORL1 variants have been associated with increased risk of Alzheimer's disease (AD), and potentially pathogenic mutations have been reported in a few early-onset autosomal dominant AD cases.

We report screening for SORL1 mutations in a Spanish cohort of cases with dementia of the Alzheimer type (DAT).

Methods: We screened for SORL1 mutations in 124 familial (44 early- and 80 late-onset) and in 15 early-onset sporadic DAT cases recruited from a referral memory clinic. Mutations found were reviewed in genomic databases, further screened for in a control population of 200 elderly subjects, and analyzed for potential pathogenicity with prediction programs (PolyPhen2 and SIFT). We also searched for segregation in the families with available siblings.

Results: Nine different potential pathogenic changes were found in ten probands (7%). Four changes had not been previously described: Trp848Ter, Arg1702Met, Gly1871Val, and splice site variant. Another five were considered very rare or rare variants (Glu270Lys, Gly852Ala, Asn1809Ser, Asp2065Val, and Ala2173Thr). After screening for these changes in the control population and available siblings, correlation with the disease (presence in at least 1/200 controls and/or no segregation) was ruled out in seven of the mutations. The change Trp848Ter and the splice-site change remained potentially pathogenic, although the study of segregation was very limited.

Conclusion: SORL1 mutations are present in 7% of our familial DAT cohort but in most cases could not be correlated with the disease process.

Disclosure: Nothing to disclose

EP2008

Cancelled

EP2009

Cancelled

EP2010

The relationship between white matter lesions and clinical features in Alzheimer's disease

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Background and aims: The purpose of this study was to determine whether in patients with Alzheimer's disease (AD), white matter lesions (WMLs) are associated with cognitive dysfunctions and the behavioral and psychological symptoms of dementia (BPSD) at initial presentation.

Methods: We retrospectively selected 73 patients with probable AD without medical history of clinical stroke. As WMLs, periventricular hyperintensity (PVH) and deep and subcortical white matter hyperintensity (DSWMH) were rated using the Fazekas scale (range, 0 to 4) on MRI imaging at initial visit. We analyzed the relationships between WMLs and clinical features including the presence of silent brain infarcts (SBIs) in basal ganglia, complication such as hypertension and scores of the Mini Mental State Examination (MMSE) and the Neuropsychiatric Inventory (NPI).

Results: Of all patients, PVH ≥ 2 (severe PVH) was found in 13 patients and DSWMH ≥ 3 (severe DSWMH) was found in 23 patients. Using multivariate analysis, severe DSWMH (OR 41.8 ; 95% CI 6.9-100< ; $p < 0.001$) was independently correlated to severe PVH. Hypertension (OR 5.9 ; 95% CI 1.4-33.1 ; $p = 0.014$), severe PVH (OR 26.2 ; 95% CI 4.7-219.4 ; $p < 0.001$) and delusion subscale of NPI (OR 1.3 ; 95% CI 1.1-1.5 ; $p = 0.014$) were independently correlated to severe DSWMH.

Conclusion: In AD, the presence of PVH did not influence clinical features, whereas the presence of severe DSWMH might show potentially serious of BPSD, especially delusions.

Disclosure: Nothing to disclose

EP2011

Age adjusted, MRI-derived normalized brain volume as a predictive biomarker of cognitive decline

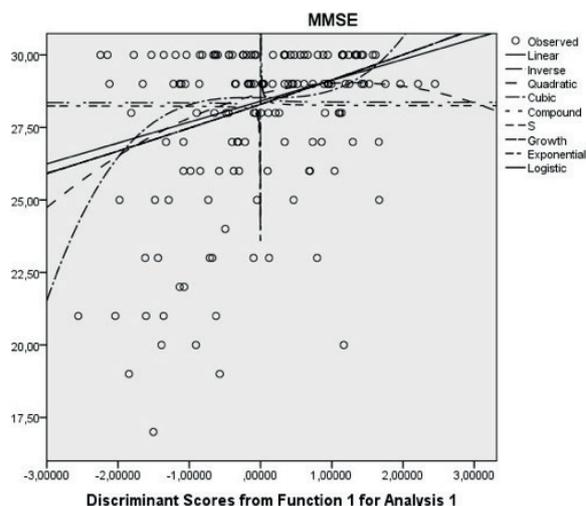
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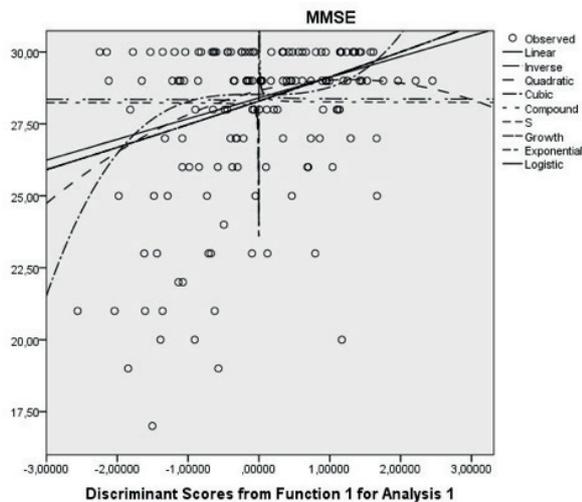
Background and aims: The objective of our study is to determine whether MRI-derived anatomical features of brain atrophy can predict cognitive impairment as measured by the Mini Mental State Examination (MMSE) scale.

Methods: In this study, we employed longitudinal data available from the Open Access Series of Imaging Studies (OASIS), (Marcus DS et al, 2009). Employing a cut-off value of 24 for the baseline MMSE, we divided the study population into the (A) normal cognition vs. (B) mild cognitive impairment groups. Subsequently, we employed derived anatomic volumes available in the OASIS dataset, namely 1. Estimated total intracranial volume (eTIV) (mm³) (Buckner et al., 2004), 2. Atlas scaling factor (ASF) (Buckner et al., 2004) and 3. Normalized whole brain volume (nWBV) (Fotenos et al., 2004) along with baseline age in order to produce a multivariate model. Multivariate analysis was performed via stepwise discriminant function analysis (DFA). Finally, curve estimation was used to determine whether a linear association existed between the DFA score and MMSE at baseline and visit 3.

Results: Stepwise DFA produced a single discriminant function, including Age and nWBV as predictors of cognitive impairment, (Wilk's lambda=0.888, $\chi^2=16.553$, $P < .0001$) achieving an overall 76% predictive accuracy. Curve estimation determined a statistically significant association between DFA score and both baseline and visit 3 MMSE score ($P < .05$).



Curve estimation for the association between baseline MMSE and DFA Score



Curve estimation for the association between visit 3 MMSE and DFA Score

Conclusion: DFA derived age adjustment on nWBV provides an easy to use biomarker predictive of cognitive impairment; the DFA predictive accuracy may be further enhanced via incorporating measurements regarding regions of interest (ROIs) into the stepwise model.

Disclosure: Nothing to disclose

EP2012

Subjective cognitive complaints in nondemented older adults relates to hippocampal atrophy as well as objective memory testing

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Background and aims: Subjective cognitive complaints (SCC) and hippocampal atrophy are potential markers of early-stage Alzheimer's disease (AD). The aim of this study was to assess the relationship between hippocampal volumes and specific SCC and to compare it to standard, routinely used memory tests.

Methods: Ninety seven non demented older adults (30 with amnesic mild cognitive impairment, 8 with non amnesic mild cognitive impairment and 59 cognitively healthy older adults) underwent comprehensive neuropsychological testing, 1.5T brain MRI scans with quantitative volumetry using FreeSurfer package to measure estimated total intracranial volume (eTIV) along with adjusted right and left hippocampal volumes, and were administered a 10-item yes/no questionnaire to evaluate SCC in the last 6 months. Spearman's correlation was used to correct for non-normal score distribution. Subjects with significant vascular changes or depression were not included.

Results: We found significant correlations of both hippocampal volumes with with the total SCC score (rR=-.19 and rL=-.22) and several items: "Difficulties with recalling past events" (rR=-.31 and rL=-.34), "Feeling of memory change" (rR=-.25 and rL=-.24) items. Left hippocampal volume correlated with "Worse memory in comparison to peers" (r=-.18) and "Subjective limitation in daily activities" (r=-.21) items. Auditory Verbal Learning Test - learning (trials 1 to 5) and delayed recall correlated with left hippocampal volume (both rs=.21). All ps' were <.05.

Conclusion: Specific SCC reflect hippocampal atrophy equally well as standard memory tests in non demented older adults and should be taken into account when identifying individuals in early-stage AD.

Disclosure: The research was supported by the project FNUSA ICRC (no. CZ.1.05/1.1.00/02.0123) from the European Regional Development Fund, by Ministry of Health, Czech Republic—conceptual development of research organization—University Hospital Motol, Prague, Czech Republic, 00064203 and by Ministry of Health of the Czech Republic, grant no. 16-27611A.

EP2013

Age- and sex-specific parental family history of dementia in relation to subclinical brain disease and risk of dementia: A population-based study

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Background and aims: Family history is an important risk factor for dementia, but the importance of age at onset and sex of the affected parent, as well as underlying mechanisms, are uncertain.

Methods: From 2000-2002, we assessed parental history of dementia in 2087 non-demented participants of the population-based Rotterdam Study (mean age 64 years, 55% female). We investigated risk of dementia (until 2015) in relation to family history, adjusting for demographics, cardiovascular risk factors, and known genetic risk variants. We furthermore determined the association between parental history and markers of neurodegeneration and vascular disease on MRI.

Results: During a mean follow-up of 12.2 years, 142 participants developed dementia. Parental history was associated with risk of dementia independent of known genetic risk factors (hazard ratio, 95% confidence interval: 1.67, 1.12-2.48), in particular when parents were diagnosed at younger age (HR, 95%CI <80years: 2.58, 1.61-4.15 versus ≥80years: 1.01, 0.58-1.77). Accordingly, age at diagnosis in probands was highly correlated with age at diagnosis in their parents <80 years ($r=0.57, p=0.001$), but not thereafter ($r=0.17, p=0.55$). Among 1161 non-demented participants with brain MRI, parental history related to lower cerebral perfusion, and higher burden of white matter hyperintensities and microbleeds. Dementia risk and MRI markers were similar for paternal versus maternal history.

Conclusion: Parental history of dementia increases risk of dementia, primarily when age at parental diagnosis is <80 years. Unexplained heredity may in part be attributed to cerebral hypoperfusion and small-vessel disease. We found no evidence of preferential maternal compared to paternal transmission.

Disclosure: Nothing to disclose

Cerebrovascular diseases 3

EP2014

Prevalence of spasticity in patients with ischemic stroke in the internal carotid artery territory – pilot results of the national SONAR registry

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Background and aims: The main aim of the study was to provide estimate of the incidence and prevalence of spasticity following stroke in the internal carotid artery territory for the regional stroke centers in the Czech Republic; the secondary goal was to identify predictors for the development of spasticity.

Methods: In a prospective cohort study, 256 consecutive patients with clinical signs of central paresis due to a first-ever stroke were examined in the acute stage. All of the patients had primary stroke with carotid origin and paresis of the upper and/or lower limb present longer than 7 days after the stroke onset. All patients were examined between 7-10 days after IS. The degree and pattern of paresis and muscle tone, the Barthel Index, baseline characteristic, and demographic data were evaluated. Spasticity was assessed using the Modified Ashworth Scale (MAS).

Results: Out of the 256 patients (157 males; mean age 69.9±12.4 years), 115 (44.9%) patients developed spasticity during the first 10 days after stroke onset. Eighty-three (32.5%) patients presented with mild neurological deficit (modified Rankin Scale 0–2) and 69 (27.0%) patients were bedridden. -024.

Conclusion: Spasticity was noted in 44.9% patients with neurological deficit due to first-ever stroke in carotid territory in the first 10 days after stroke onset. Severe spasticity was rare.

This study was partially supported by the Czech health research council of the Ministry of Health of the Czech Republic no. 15-31921A and by a grant from the Internal Grant Agency of Palacky University LF-2017-024.

Disclosure: This study was partially supported by the Czech health research council of the Ministry of Health of the Czech Republic no. 15-31921A and by a grant from the Internal Grant Agency of Palacky University LF-2017-024.

EP2015

Associations of common carotid artery intima-media thickness with risk factors for stroke in the population of Republic of Moldova.

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Background and aims: Increased common carotid artery intima-media thickness (CCA-IMT) is associated with an increased risk of stroke. We studied the relationships between CCA-IMT and stroke risk factors in the population of Republic of Moldova. Here we present preliminary results of the National State Programme joined to International Project "Primary Stroke Prevention".

Methods: The included subjects were examined according to a pre-established International Protocol of risk factors' estimation, which included non-invasive measurements of average CCA-IMT from left and right side (B-mode ultrasonography), questionnaire, clinical and laboratory examination.

Results: In this study were enrolled 300 subjects, among which 180 (60%) were women and 120 (30%) men (age 49.91±14.5 years). We found significant associations between CCA-IMT and several clinical and laboratory variables. CCA-IMT significantly correlated with systolic ($r=0.43$, $p=0.00$) and diastolic ($r=0.34$, $p=0.00$) blood pressure, body mass index ($r=0.40$, $p=0.00$), abdominal circumference ($r=0.46$, $p=0.00$), glycated haemoglobin ($r=0.24$, $p=0.00$), total cholesterol ($r=0.14$, $p=0.01$), LDL-cholesterol ($r=0.20$, $p=0.00$), HDL-cholesterol ($r=-0.18$, $p=0.00$) and fibrinogen ($r=0.24$, $p=0.00$).

Conclusion: Increased thickness of intima-media of the carotid artery is associated significantly with other traditional risk factors for stroke. Thus, CCA-IMT can be considered an early common integrator of the effects of multiple risk factors on the arterial wall.

Disclosure: Nothing to disclose

EP2016

Addenbrooke's cognitive examination in nondemented patients after stroke

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Background and aims: The aim of study is compare cognitive functions in nondemented stroke patients 3-6 month after stroke, with sex and age matched nondemented and nondepressed controls, by Addenbrookes' Cognitive Examination.

Methods: Totally 156 respondents, 72 healthy controls (19 men, mean age 64.5±12.4 years) and 84 patients after stroke (54 men, average age 62.2±9.0 years) were tested.

Results: Statistically significant difference between healthy controls and stroke patients in total score of Addenbrookes' Cognitive examination (Stroke patients' score 86.2 points, Healthy controls' score 91.2 points, $p<0.01$), Verbal Production domain (stroke patients' score 9.8 points, healthy groups' score 11.5 points, $p<0.01$) and Memory domain (stroke patients' score 19.5 points, healthy groups' score 21.7 points, $p<0.01$) were demonstrated. The difference was statistically significant also between the both stroke patients subgroups: A/ patients with right-sided brain lesion and healthy controls in the total score (88.3 vs. 91.3 points, $p<0.05$) and Verbal Production (9.9 vs. 11.5 points, $p<0.01$) were demonstrated and B/ left-sided brain lesion and healthy controls in total score (83.9 vs. 91.3 points, $p<0.01$), domains Memory (18.6 vs. 21.7 points, $p<0.01$) and Verbal Production (9.6 vs. 11.5 points, $p<0.01$).

Conclusion: This study shows the decline in cognitive functions tested using Addenbrookes' Cognitive Examination in stroke patients 3 – 6 month after stroke.

Disclosure: Supported by institutional support NO. 1 RVO-FNOs/2012 1.7.2012 - 1.7.2015.

EP2017

The role of contralesional motor areas in the first days after stroke – an fMRI-guided TMS-study

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Background and aims: Neuroimaging studies have demonstrated that after stroke a number of areas in the contralesional hemisphere show increased activity when patients move their affected hand (Rehme et al., 2012). While some studies suggest a supportive role of these regions during stroke recovery (Lotze et al., 2006), others point to a maladaptive role (Nowak et al., 2008).

Methods: We here tested the functional relevance of activation changes in contralesional M1, dorsal premotor cortex (dPMC) and anterior intraparietal cortex (aIPS) in early subacute stroke patients. Activity was assessed by fMRI and subsequently disturbed using trains of 10Hz rTMS time locked to hand motor tasks. Motor performance was measured using a 3D motion analyser system. Imaging data were analyzed using SPM8.

Results: Online-TMS over the individual fMRI maxima led to differential effects on motor performance. TMS interference with contralesional M1 and dPMC normalized movement fluency in patients showing higher activation during paretic hand movement. Moreover, TMS-interference with contralesional aIPS led to an increase of tapping amplitude and peak velocity across the patient group.

Conclusion: In conclusion, online-TMS over higher activations of M1 and dPMC improved patients' motor fluency, whereas online-TMS over aIPS improved spatial aspects of movements. Thus, the present results suggest a disturbing influence of all examined regions on different features of movement kinematics already during the first days after stroke in mildly to moderately affected patients.

Disclosure: Nothing to disclose

EP2018

Posterior Reversible Encephalopathy Syndrome (PRES): A disease with a broad clinical and radiological spectrum

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Background and aims: PRES is a disease related to specific entities that affect the cerebral blood flow regulation. The aim of this study is to analyze the epidemiological and clinical features, as well as the outcome of patients diagnosed with PRES in our institution.

Methods: Retrospective observational study of patients diagnosed with PRES and assessed by neurologist in our hospital between the years 2010-2016. Demographics, medical background and previous treatments, clinical features at income, diagnostic test results and clinical outcome were recorded.

Results: Among the 14 patients included, 50% (n=7) were woman, with an average age of 52.7 years old (range 3-80). In the medical background found as trigger were high blood pressure in 43% (n=6) of cases (BP at income 183/95mmHg, SD 53/30mmHg) and immunosuppressive therapy, 43% as well. The main clinical manifestation was epileptic seizure, 71% (n=10): 50% (n=5) generalized tonic-clonic type and 10% (n=1) epileptic status. 60% (n=6) required ≥ 2 antiepileptic drugs and 10% required iv sedation. The second most common manifestation were visual alterations, 43% (50% (n=3) had binocular blindness). Among de imaging findings 86% (n=12) were atypical (unilateral, asymmetrical and non parieto-occipital). 43% of patients experienced some complication, 33% (n=2) of them neurological (hemorrhage and epileptic status). In the outcome 86% were fully recovered by 3 months and only 14% (n=2) were dead (of non-neurological causes).

Conclusion: PRES affects patients of any age and gender with wide clinical and radiological features, being epileptic seizures and “atypical” images the most common ones. It’s not always reversible, exclusive of white matter or posterior.

Disclosure: Nothing to disclose

EP2019

What would happen if all stroke patients arrived within the therapeutic window for thrombolysis?

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Background and aims: In the last years, many efforts have been made to increase thrombolysis rates. Media campaigns, prenotification systems and hospital reorganization have been developed with varied success. Anyway, thrombolysis rates are still low. Studies addressing eligibility in patients excluded from reperfusion therapies because of exceeded therapeutic window are scarce.

Methods: Patients attended in the Emergency Department with a final diagnosis of stroke or TIA from November 2013 to January 2015 were included. Data on PD, treatment applied and exclusion criteria for thrombolysis (if present) were recorded. A descriptive analysis of the reasons for exclusion from thrombolytic treatment was performed

Results: 382 patients were included. 197 (51.57%) had a PD>3h. One received rt-PA (0.51%). 196 were excluded. 104 of them (53.06%) were asymptomatic or paucisymptomatic at arrival, 22 (11.22%) became asymptomatic before treatment decision, 18 (9.18%) were excluded because of CT findings, 13 (6.63%) because of poor functional status and 3 (1.53%) showed INR>1.7. 36 patients (18.36%) would have been eligible if the therapeutic window hadn't been exceeded. 29 (14.8%) had a PD>4.5h, 6 (3.06%) because of in-hospital delays and one (0.51%) because of unknown onset.

Conclusion: Most patients arriving after the first three hours do it asymptomatic or paucisymptomatic, or symptoms resolve spontaneously before thrombolitics are administered, but some of them would have been treated – with prognostic implications – with a sooner arrival, as would some of those excluded because of CT findings. Still many patients remain untreated only because of an exceeded therapeutic window. They should be the target for future campaigns.

Disclosure: Nothing to disclose

EP2020

Pelvic deep venous thrombosis in patients with cryptogenic stroke and patent foramen ovale

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Background and aims: Paradoxical embolism from pelvic deep vein thrombosis (DVT) has been suggested in several studies as a mechanism of ischemic stroke in patients with patent foramen ovale (PFO) and cryptogenic stroke. Performing a pelvic magnetic resonance venography (MRV) as part of an inpatient diagnostic evaluation has been recommended.

Methods: Adult patients with ischemic stroke and PFO who underwent pelvic MRV and lower extremity (LE) duplex ultrasound as part of the diagnostic evaluation were included in this single-center retrospective observational study, between 2006-2015, to determinate DVT prevalence as a possible source of paradoxical embolism.

Results: Of 81 patients with ischemic stroke and PFO (male sex 57%, median age 55 years), 49 were diagnosed with cryptogenic stroke (male sex 55%, median age 50 years). Deep vein thrombosis imaging study was performed in 80% of patients, 95% with LE duplex ultrasound and 51% with pelvic MRV. DVT prevalence in cryptogenic stroke patients was 8.2% (4 patients), 3 of them had LE thrombosis (6.1%) and 1 had pelvic DVT (2.0%). All these patients had a normal hypercoagulability testing. There was no significant difference in the prevalence of pelvic DVT in patients with PFO and non-cryptogenic stroke.

Conclusion: Our results differ from those of the PELVIS Study (20% pelvic DVT prevalence) and are similar to more recent studies which find a lower prevalence of pelvic DVT in patients with PFO and cryptogenic stroke. We think routine inclusion of pelvic magnetic resonance venography in the diagnostic evaluation of this subtype of patients cannot currently be recommended and needs further investigation.

Disclosure: Nothing to disclose

EP2021

Endovascular treatment of cerebral venous sinus thrombosis

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Background and aims: Anticoagulation is the standard treatment for cerebral venous sinus thrombosis (CVST). However, neurological condition may worsen during anticoagulation especially in cases with extensive thrombosis. Endovascular treatment (ET) may be considered in these selected cases. The aim of this study was to report our experience with ET in severe cases of CVST.

Methods: In this retrospective case series, we report the clinical and radiological outcomes of 11 CVST patients treated with endovascular methods at our institution between July 2010 and February 2016.

Results: The mean age (10 female, 1 male) was 28 years (17-45). All patients received intravenous heparin initially. The most frequent indication requiring ET was worsening or no improvement in mental status despite treatment. Mean GCS before ET was 11.2±0.6. Balloon venoplasty was used in six patients, suction thrombectomy in five and stent-retriever thrombectomy in one. All patients received local intrasinus thrombolytic therapy with t-PA (5-40 mg). Clinical stabilization or rapid clinical improvement observed within 1-3 days of ET. Patients' mean GCS reverted to 15 at discharge. Discharge modified Rankin scale (mRS) scores were 1 in seven patients, 2 in one and 3 or over in three. Eight patients scored below 2 at one month and nine patients scored below 1 at long-term follow-up (6-48 months).

Conclusion: Although there are no randomized controlled trials, ET may be considered in carefully selected cases with more severe clinical condition, with worsening or no improvement despite anticoagulation. Randomized controlled trials are required to provide the evidence of endovascular treatment effect in CVST patients.

Disclosure: Nothing to disclose

EP2022

Polymorphisms of platelet von Willebrand factor receptor gene in patients with atherothrombotic and lacunar stroke

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Background and aims: Receptors of von Willebrand factor (vWFR) are on second place according to density on platelets. Experimental vWFR inhibition demonstrated promising results for cerebral ischemia manifestation prevention on animals.

Aim of study - reveal association between vWFR polymorphisms and age of atherothrombotic stroke (ATS) and lacunar infarction (LI) occurrence.

Methods: We examined patients with uncomplicated ATS and LI. Type of stroke in all patients was verified by clinical, neuroimaging and laboratory investigation. Patients were distributed on 2 subgroups: I –18-60 years in men, 18-55 years in women, II—from 61 years in men/55 years in women till 74. Genetic tests to detect c.3550C>T and T(-5)C polymorphisms into gene coding vWFR alpha-chain were performed. Confidence interval (CI) of frequencies was detected using angular transformation, relative risk (RR) was calculated by usual formula.

Results: Polymorphism frequencies are shown in tables 1 and 2. Presence of c.3550C>T mutation predispose to stroke in younger age – RR for ATS was 2.1 (95%CI 1.6–2.9), RR for LI – 2.0 (95% CI 1.1–3.6). Such mutation results in vWFR activity increasing. Presence of T(-5)C polymorphism predispose to ATI in younger age with RR 2.1 (95%CI 1.5–2.9) and there was no frequency difference in LI subgroups. T (-5)C polymorphism is connected with increased density of vWFR upon platelet surface.

Table 1. Frequency of mutant allele for c.3550C>T

Group	Age subgroup	
	I	II
ATS	24,7% (95% CI 18,1–32,0) n=73	6,0% (95% CI 2,9–10,1) n=83
LI	14,1% (95% CI 7,8–21,9) n=46	4,3% (95% CI 2,0–7,5) n=104

Table 2. Frequency of polymorphisms for T(-5)C

Group	Age subgroup	
	I	II
ATS	21,9% (95% CI 15,6–29,0) n=73	6,6% (95% CI 3,3–10,9) n=83
LI	22,8% (95% CI 14,9–21,9) n=46	24,1% (95% CI 18,5–30,1) n=104

Conclusion: Presence of abnormalities into gene, coding alpha-chain of Ib platelet receptor, predispose to younger age of stroke occurrence. Further investigation is required to reveal influence of hereditary changes in platelet vWFR to different stroke variants.

Disclosure: Nothing to disclose

EP2023

GLA p.A143T variant Fabry disease may result in a severe phenotype with extensive microvascular cerebral involvement at a young age

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Background and aims: Fabry disease (FD) is a rare inborn error of glycosphingolipid catabolism that results from the deficient activity of the lysosomal enzyme alpha-galactosidase A (AGAL-A). Genetic screening studies have revealed over 600 variants in the galactosidase alpha (GLA) gene. The p.A143T variant is a genetic variant of unknown significance (GVUS), with its associated phenotype ranging from classical FD to healthy unaffected patients. Some authors however deem this variant non-pathogenic.

The aim of this case report is to describe the case of a 16-year-old male with multifocal white matter lesions on brain MRI performed in the diagnostic workup for episodic headaches, who was diagnosed with Fabry disease.

Methods: Available demographical, clinical and ancillary investigations were reviewed.

Results: A 16-year-old male presented with episodic headaches and an MRI that showed multifocal punctate to patchy white matter lesions (Figure 1, 2 and 3). Past medical history revealed a period of absence-like episodes at the age of 10, with normal EEG. The diagnosis of FD was suggested upon the finding of significantly reduced plasma AGAL-A activity (0.62µmol/L or 13% of normal; normal range ≥1.65µmol/L) and genetic investigation confirmed the presence of a hemizygous missense variant in the GLA gene (p.A143T). Baseline assessment of systemic involvement showed only a discrete proteinuria.

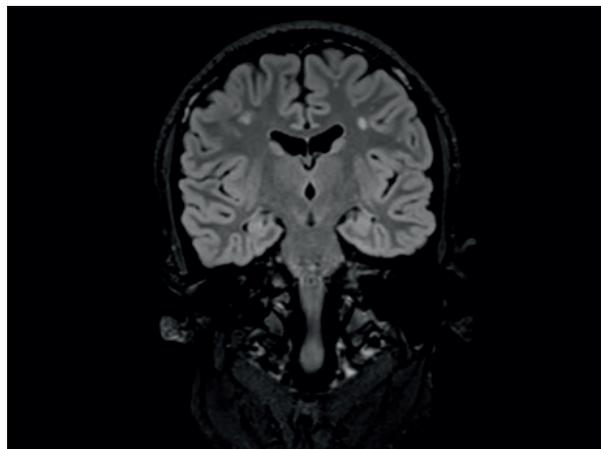


Figure 1

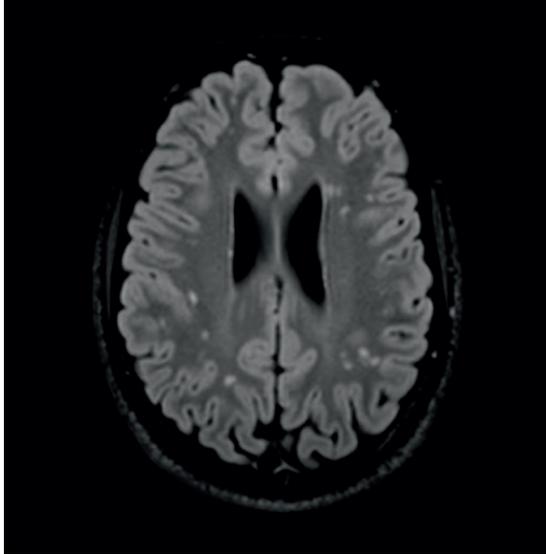


Figure 2

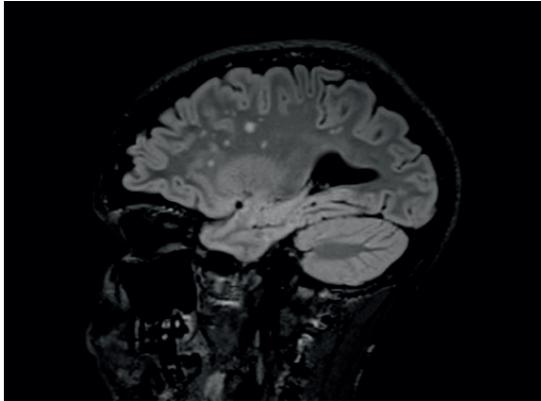


Figure 3

Conclusion: A diagnosis of FD should be considered when finding asymptomatic extensive cerebral white matter lesions in a young patient. Furthermore, the causative p.A143T mutation can be associated with a more severe subclinical phenotype than has been reported to date.

Disclosure: Nothing to disclose

EP2024

Dural arteriovenous fistula with transient memory loss and cognitive decline treated with endovascular embolization

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Background and aims: Dural arteriovenous fistula (DAVF) is an uncommon intracranial vascular malformation, which is accompanied by significant morbidity and mortality. Though true incidence of DAVF is unknown, reported incidence is approximately 10-15% of all intracranial vascular abnormalities. Clinical manifestations of intracranial DAVF are various including pulsatile tinnitus, orbital congestion, headache, intracranial hemorrhage or infarction. However, there have been little reports about DAVF manifested as rapidly progressive dementia.

Methods: A 43-year-old male presented daytime sleepiness at work and indifferent behavior like never before. Two weeks later, he had episodic memory loss with well preserved remote memory. Brain MRI showed thrombus and dural arteriovenous fistula in right lateral transverse sinus with bilateral thalamic venous infarction. Cerebral angiography confirmed right transverse sigmoid dural arteriovenous fistula with feeding artery of right occipital artery and left posterior meningeal artery.

Results: Multiple transarterial embolization was done successfully and patient returned back to his daily life.

Conclusion: Recently endovascular treatment have become one of the main therapeutic options to obliterate the fistulous site. They have led rapid diagnostic approach and management of DAVF with high curative rates. We report a rare case of dural arteriovenous fistula which caused rapidly progressive dementia successfully treated by endovascular approach.

Disclosure: Nothing to disclose

EP2025

Cancelled

EP2026

Long-term outcome and secondary prevention of cardioembolic stroke in severely disabled patients

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Background and aims: Unfavorable functional outcome after stroke is considered a reason not to anticoagulate patients for secondary stroke prevention.

Methods: A score of 4-5 in modified Rankin scale is considered a bad functional stroke outcome. A prospective study included 167 severely disabled cardioembolic stroke survivors discharged from P. Stradins Clinical University Hospital, Riga, Latvia in 2015. Patients or their relatives were interviewed by phone 365 days after leaving the hospital. Standardized questions were asked about patient abilities. The results were compared in patient groups according to prescribed medication.

Results: The average one-year mortality was 52,08%. The functional outcome according to prescribed medication is shown in table below.

mRs	Outcome 90d after discharge			Outcome 365d after discharge		
	0-3	4-5	6	0-3	4-5	6
No antithrombotic (n=15)	0,0%	13,3%	86,7%	0,0%	13,3%	86,7%
Antiplatelet agents (n=79)	10,1%	26,6%	63,3%	12,7%	8,9%	78,5%
VKA (n=17)	29,4%	29,4%	41,2%	41,2%	11,8%	47,1%
NOACs (n=56)	57,1%	19,6%	23,2%	57,1%	12,5%	30,4%

Conclusion: One-year mortality of severely disabled patients is high. But as the functional outcome is improving in one year after the stroke and mortality rate is significantly lower in patient groups started on oral anticoagulants, these patients with unfavorable stroke outcome at time of discharge should not be denied oral anticoagulants for secondary stroke prevention.

Disclosure: Nothing to disclose

Cerebrovascular diseases 4

EP2027

Cerebral venous thrombosis associated with use of erythropoietin as a performance-enhancing drug: A case report

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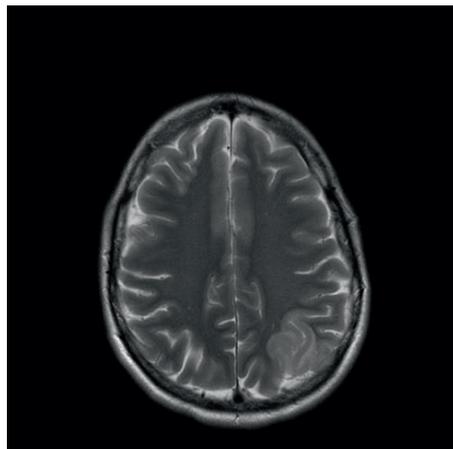
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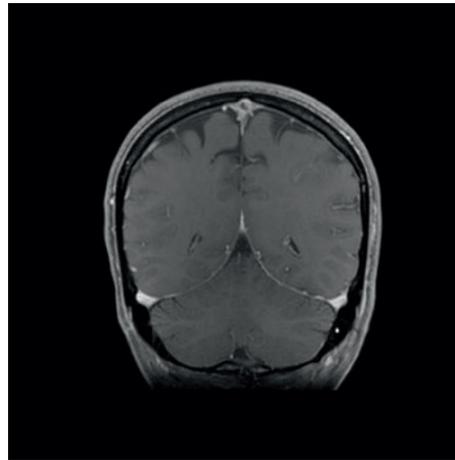
Background and aims: Central Venous and Sinus Thrombosis (CVST) is a rare and under-diagnosed type of cerebrovascular disease which is more prevalent in young women and often correlated with a pro-thrombotic state; only three case reports have correlated it with use of erythropoietin, two of which as treatment for chronic kidney disease. Our aim is to report a second case of erythropoietin use as doping as contributing factor for CVST.

Methods: Case report, with review of the pertinent literature.

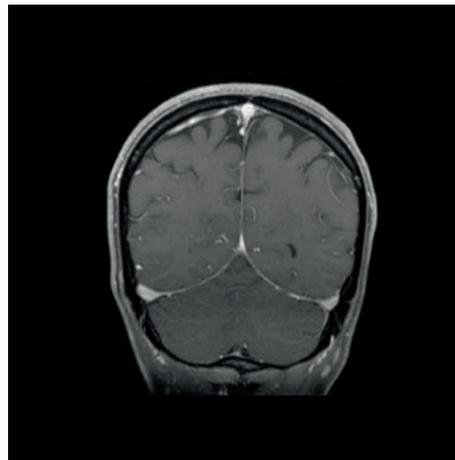
Results: A 38-year-old female professional cyclist without prior history presented to the emergency room after two episodes of seizure in the same afternoon. Her physical examination was unremarkable. The head CT scan without contrast showed no abnormalities. As blood analysis demonstrated a globular volume of 50.35% and hemoglobin of 17.39g/dL, cerebral venous thrombosis was suspected and brain MRI was performed, which showed thrombotic occlusion of the superior sagittal sinus and superficial cortical veins, such as the left vein of Trolard. She admitted to the use of erythropoietin as doping, which was associated with her hemogram alterations. Treatment with warfarin was initiated while in the hospital, and follow-up consultations showed complete clinical recovery. A new MRI performed six months after the initial presentation showed recanalization of the venous structures.



T2-weighted brain MRI demonstrating the area of venous infarction caused by the thrombosis



Coronal slice of a T1-weighted brain MRI demonstrating the occlusion of the superior sagittal sinus after the injection of gadolinium-based contrast



Comparative coronal slice of a T1-weighted brain MRI performed five months afterwards demonstrating recanalization of the superior sagittal sinus

Conclusion: In the investigation of patients presenting with seizures and pro-thrombotic states, such as use of erythropoietin, cerebral venous thrombosis should always be considered.

Disclosure: Nothing to disclose

EP2028

Memory impairment due to bilateral fornix infarction: Characterisation and follow-up

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Background and aims: The fornix is an important structure regarding consolidation of new data into long term memory.

Methods: We report the case of a patient with bilateral fornix infarction, and the results of a 7-month follow-up with neuropsychological evaluation.

Results: A 68-year-old woman had a scheduled, endovascular intervention on a non-ruptured aneurysm of the anterior communicating artery. There were no immediate complications. On the next day, topographic disorientation, repetitive, and digressive speech were noticed. Brain-MRI showed an acute infarction of both anterior fornix pillars, more pronounced on the right side, with a below-centimetre parietal injury. Neuropsychological evaluation documented a severe anterograde memory deficit, involving verbal, visual, and topographic components, with normal working, autobiographic and remote semantic memories testing. Seven months later, the patient maintained a considerable functional impairment (examples, not being able to memorize new routes, unable to read books due to difficulty in remembering elements of the story line), but a substantial improvement in verbal and visual anterograde memory tests.

Conclusion: To our knowledge, a single case with a similarly extended and detailed cognitive follow-up was published, referring to a patient with subarachnoid, intraventricular and intracerebral haemorrhages. In our case, MRI showed a clear anatomical and etiologic definition of the fornix injury, which allowed a more accurate cognitive assessment, and follow-up. These revealed a significant improvement regarding verbal and visual episodic memories.

Disclosure: Nothing to disclose

EP2029

The effect of alpha-lipoic acid supplementation on anthropometric indices and food intake in patients experienced stroke: A randomized, double blind, placebo-controlled clinical trial

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Background and aims: Stroke as a devastating condition is a major cause of death worldwide and accountable for long time disability with high personal and social cost in adults. Metabolic syndrome and obesity are well known risk factors of coronary artery disease, stroke, and mortality. Alpha-lipoic acid (ALA) is an eight-carbon, sulfur-containing compound with antioxidant properties which reduces body weight, changes other anthropometric indices and regulate food intake by suppressing appetite and increasing metabolism. This study was designed to evaluate the possible effects of ALA supplementation in patients with stroke.

Methods: In this randomized, double blind, placebo-controlled clinical trial, sixty-seven patients with stroke were randomly allocated to two groups (taking a 600 mg ALA supplement or placebo daily for 12 weeks). Weight, waist circumference, energy, carbohydrate, protein and fat intake were measured and body mass index was calculated before and after intervention in this study. Dietary intake and statistical analyses were carried out using N4 and SPSS16 software, respectively.

Results: Primary features were similar in the intervention and placebo groups ($p < 0.05$). After the intervention period, waist circumference ($p < 0.001$), energy, carbohydrate, protein and fat intake ($p < 0.001$) decreased significantly in ALA group compared with placebo. While no differences were observed in weight ($p = 0.26$) and BMI ($p = 0.56$) in ALA supplementation group compared with placebo.

Conclusion: Results of this trial indicated that 12 weeks supplementation with 600 mg alpha-lipoic acid has beneficial effects on anthropometric indices (weight, body mass index, waist circumference) and food intake (energy, carbohydrate, protein, and fat) in patients with stroke.

Disclosure: Isfahan university of Medical sciences supported this research.

EP2030

Remote symptomatic intracerebral haemorrhage post intravenous thrombolysis

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Background and aims: Intracerebral hemorrhage (ICH) after treatment with intravenous recombinant tissue-type plasminogen activator (rtPA) for ischemic stroke can occur in local relation to the infarct, as well as in brain areas remote from infarcted tissue. Remote intracerebral haemorrhage (rICH) is ICH post thrombolysis in brain regions without visible ischaemic changes. To date, it is proposed possible influence of cerebral amyloid angiopathy which may contribute to rICH.

Methods: We report a case of 67-year-old gentleman, with history of metastatic non small cell lung cancer to bone, unknown cerebral metastasis, presented with sudden onset of slurred speech and mild hemiparesis. Clinical evaluation revealed Left Middle Cerebral Artery infarct with aphasia and mild right hemiparesis. Urgent CT Brain and CT Angiogram of the Circle of Willis and Carotid Arteries showed Left M1/ M2 junction occlusion. Patient was given intravenous rtPA at the dose of 0.9mg/kg and he underwent endovascular therapy. The procedure was uneventful.

Results: Noted dropped in Glasgow Coma Scale from 15 to 3 after 1 hour post procedure. Urgent CT Brain done showed large right cerebral haematoma with midline shift and early hydrocephalus. Patient eventually passed away.



CT Brain on admission



CT Angiogram



CT Brain post IV Thrombolysis

Conclusion: rICH is an uncommon complication of intravenous thrombolysis that increases the risk of poor neurological outcome and mortality. In this case, in view of relatively young patient with no significant cardiovascular risk factors (diabetes mellitus, hypertension, hyperlipidaemia), there maybe a possibility of micro-cerebral metastasis that was not seen in the plan CT Brain done on admission, which potentially may account for rICH.

Disclosure: Nothing to disclose

EP2031

Abdominal diameter index as a predictor of early neurological deterioration in acute ischemic stroke

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Background and aims: Early neurological deterioration (END) occurs frequently in acute ischaemic stroke. The abdominal diameter index (sagittal abdominal diameter/thigh circumference, ADI) has been shown to predict the cardiovascular disease related with visceral obesity and insulin resistance. To determine the ADI as a predictor of END in acute ischaemic stroke.

Methods: We analyzed 657 consecutive patients with acute ischaemic stroke within 24 hours of symptom onset using a single center registry of maintained clinical data including abdominal diameter index. Major stroke etiologies were divided into cardioembolic, large vessel, small vessel, other, and unknown origins. END was defined as a worsening 2 or more points deterioration on the National Institutes of Health Stroke Scale(NIHSS) during 5 days of hospitalization. Stepwise regression models were generated to associate clinical factors with END.

Results: Of the included 657 patients (median age 68 years, 54% male), 211(32%) experienced END. END was associate with lower NIHSS score on admission ($P<0.01$), higher glycemia ($P=0.04$), larger mismatch volume ($P=0.01$), and proximal artery occlusion ($P=0.03$). Stroke with large vessel disease were associated with a twofold higher odds of END in stepwise regression models (OR 2.0, 95% CI 1.2-6.4, $P=0.001$). In a logistic regression analysis controlling for other cardiovascular risk factors including age, smoking, total cholesterol, high-density lipoprotein cholesterol, triglycerides, blood pressure and glucose, ADI were significantly associated with END in large vessel disease ($p<0.04$).

Conclusion: ADI may be an anthropometric predictor for END in acute ischemic stroke patients with large vessel disease.

Disclosure: Nothing to disclose

EP2032

Cancelled

EP2033

Pre-stroke depression symptoms are not associated with an increased risk of delirium in the acute phase of stroke

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Background and aims: Delirium is an acute cognitive disorder that affects between 10% and 48% of patients after stroke and it associated with worse outcome. Depression can precede, coexist or follow the episode of delirium. It was suggested that these two syndromes could share common pathophysiological mechanisms including monoamine transmission and inflammatory reaction. The link between delirium and depression can be seen only in certain populations such as postoperative patients. We aimed to determine association between pre-stroke depression symptoms and risk of post-stroke delirium.

Methods: We recruited patients with stroke or transient ischemic attack admitted within 48 hours from symptoms onset. We assessed delirium on a daily basis during the first 7 days of hospitalization. Diagnosis of delirium was based on DSM-5 criteria. We assessed pre-stroke depression symptoms using depression item from Neuropsychiatric Inventory.

Results: We included 606 patients (median age: 73, 53% female). We diagnosed delirium in 171 patients (28.2%). In logistic regression, we compared upper quartile of depression score to other quartiles. On univariate analysis, higher score of depression was associated with increased risk of delirium (OR 1.58, 95%CI: 1.04-2.40, $P=0.03$). However, after adjustment for possible confounders: age, atrial fibrillation, diabetes mellitus, stroke severity, pre-stroke cognitive decline, pre-stroke disability, pneumonia and urinary tract infection, this relation did not remain significant.

Conclusion: Pre-stroke depression symptoms are not an independent predictor of delirium in the acute phase of stroke.

Disclosure: The Leading National Research Centre of Medical Faculty of Jagiellonian University funded the collection of data for the study.

EP2034

Pre-stroke cognitive impairment and the course of post-stroke delirium– analysis of delirium duration, symptoms severity, fluctuations and change in cognition

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Background and aims: Cognitive impairment is a widely recognized risk factor for delirium. Patients with impaired cognition might have more severe delirium due to diminished cognitive reserve. However, it is not clear how pre-existing cognitive impairment is related to other features of delirium including duration, symptoms fluctuations and change in cognition. We aimed to determine association between pre-stroke cognitive impairment (PSCI) and features of post-stroke delirium: symptoms severity and fluctuations, duration and change in cognition.

Methods: We assessed delirium on a daily basis during the first 7 days of hospitalization. Diagnosis of delirium was based on DSM-5 criteria. To assess PSCI we used Informant Questionnaire on Cognitive Decline in Elderly. We used measures based on Cognitive Test for Delirium and Delirium Rating Scale-Revised-98 to assess severity and fluctuations of delirium symptoms. Severity measures included: mean score, peak score, sum of scores. Fluctuations were measured as a change in delirium scores. We calculated change in cognition as a difference between two Montreal Cognitive Assessment scores (done on day 1-2 and day 7-10).

Results: We included 610 patients with stroke or transient ischemic attack. We diagnosed delirium in 171 patients (28%). Among them 60 (35.1%) had PSCI. Patients with PSCI scored worse in all delirium severity measures. There was no difference in delirium duration, symptoms fluctuations and no difference in change in cognition during delirium episode between patients with and without PSCI.

Conclusion: Pre-stroke cognitive impairment is associated with the severity of post-stroke delirium but not with delirium duration, symptoms fluctuations and change in cognition.

Disclosure: The Leading National Research Centre of Medical Faculty of Jagiellonian University funded the collection of the data for the study.

EP2035

The effectiveness of acupuncture treatment on cerebral vasospasm after aneurysmal subarachnoid haemorrhage

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Background and aims: The purpose of this study is to assess the effectiveness of acupuncture treatment on cerebral vasospasm after aneurysmal subarachnoid hemorrhage (aSAH).

Methods: A double-blind, randomized placebo-controlled trial of acupuncture was conducted. Thirty-two patients with aSAH who had undergone aneurysm clipping or coil embolization within 96 hours of onset were enrolled. Participants received combined therapy consisting electroacupuncture and intradermal acupuncture or sham acupuncture, once a day for 2 weeks. The incidence of delayed ischemic neurologic deficit (DIND), angiographic vasospasm, TCD vasospasm and vasospasm-related cerebral infarction were evaluated for 2 weeks. After 2 weeks or at discharge, mortality and rate of subjects who recovered mRS were also examined. Serum nitric oxide (NO) and endothelin-1 (ET-1) concentration were measured.

Results: The incidence of DIND was not significantly different between two groups. The incidence of angiographic vasospasm in the treatment group was lower than the control group. The incidence of vasospasm-related cerebral infarction in the treatment group was lower than the control group. The percentage of subjects who recovered as mRS ≤ 2 at 2nd flow up (4 weeks or discharge) was higher in the treatment group than in the control group.

For both serum NO and ET-1 level, there was a significant difference during 2 weeks only in non-vasospasm group, not in vasospasm group. After 2 weeks' intervention, there was a significant increase in the level of NO in the treatment group.

Conclusion: Acupuncture had a tendency to improve the incidence of DIND, angiographic vasospasm, vasospasm-related cerebral infarction and functional recovery.

Disclosure: Nothing to disclose

EP2036

Cancelled

EP2037

Stroke and TIA mimics in patients referred to a neurological emergency department by outpatient physicians, ambulance physicians and paramedics

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Background and aims: Our aim was to compare the structure and management of conditions mimicking acute cerebrovascular events (ACE, stroke or transient ischaemic attack) between patients referred directly to neurological emergency department (ED) by outpatient physicians, ambulance physicians and paramedics.

Methods: We analyzed consecutive patients referred to a Polish urban neurological ED with suspicion of ACE between 1st January 2014 and 31st December 2014.

Results: There were 128 ACE mimics referred by outpatient physicians, 61 by ambulance physicians and 67 by paramedics. Compared to the other groups, patients referred by outpatient physicians were significantly younger (median age 66 vs 72 and 73 years), more often female (70.3% vs 54.1% and 56.7%) and with negative history of ACE (80.5% vs 63.9% and 74.6%). We found no significant differences in the history of epilepsy, type of ACE stated on referral, need for neuroimaging in ED, and ratios of neurological to non-neurological ACE mimics (35:93, 22:39, 28:39). However, patients referred by outpatient physicians had a distinct structure of final diagnoses within both neurological (frequent headaches) and non-neurological (frequent very high blood pressure) mimics. The proportion of admissions to a neurological ward despite having ACE mimics in referrals from ambulance physicians was higher than from outpatient physicians (42.6% vs 20.3%, $p=0.001$) and tended to be higher compared to paramedics (26.9%, $p=0.061$).

Conclusion: The structure of ACE mimics differs between referrals from outpatient physicians and ambulance physicians or paramedics. However, the need for urgent neurological admission appears to be high only in patients referred by ambulance physicians.

Disclosure: Nothing to disclose.

EP2038

Cancelled

EP2039

A benign presentation of inflammatory cerebral amyloid angiopathy

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Background and aims: Inflammatory cerebral amyloid angiopathy (CAA-ri) is a rare form of meningoencephalitis, presenting with encephalopathy in the majority of patients (74%). Even with immunosuppressive therapy, the mortality rate is 33%. We present a case that had a benign presentation with transient symptoms and a full spontaneous recovery.

Results: A 62-year-old-man with a history of hypertension presented in the emergency room with a transient episode of spreading left hemisensory disturbance lasting few minutes. Brain CT scan disclosed a right temporoparietal hypodensity. Brain MRI showed a right temporoparietal white matter lesion, hyperintense on T2-weighted sequences and multiple bilateral corticosubcortical microbleeds in T2*. ApoE genotype was $\epsilon 4 / \epsilon 4$. A diagnosis of probable CAA-ri was assumed. Given that the patient remain asymptomatic since admission, a conservative approach was adopted, and steroid therapy and biopsy was postponed. One month later, the patient remained asymptomatic and the MRI showed an almost complete reversion of the temporoparietal lesion while the microbleeds were stable. He remained asymptomatic the following year.

Conclusion: The presented case is consistent with a probable CAA-ri. The presentation with mild, transient and reversible symptoms suggests that this entity might be underdiagnosed.

Disclosure: Nothing to disclose

Cerebrovascular diseases 5

EP2040

Elaboration of new model for predicting early clinical deterioration in patients with acute spontaneous supratentorial intracerebral hemorrhage and secondary intraventricular hemorrhage

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Background and aims: Predicting early clinical deterioration (ECD) in patients with acute spontaneous supratentorial intracerebral hemorrhage (ASSICH) and secondary intraventricular hemorrhage (IVH) is a very important and relevant in modern angioneurology, that can help the practitioners choose optimal treatment approaches to improve its efficacy. The aim was elaboration new statistical model for predicting early clinical deterioration (ECD) in patients with ASSICH and secondary IVH.

Methods: 69 patients (mean age 64.4 ± 1.5 years) were studied during first 24 hours after clinical onset of the disease. Clinical examination included vital signs verification and evaluation by National Institute of Health Stroke Scale, Glasgow Coma Scale, Full Outline of UnResponsiveness (FOUR). Early clinical deterioration was verified in patients with decrease FOUR score ≥ 1 during 24 hours from the beginning of the disease. Severity of IVH was verified by IVH score (IVHS) using parameters of computer tomography. Secondary IVH volume (IVHV) was calculated by formula: $IVHV (mL) = e^{(IVHS \text{ score}/5)}$. Elaboration of prognostic model was made by logistic regression and ROC-analysis.

Results: Out of 69 patients, 19 (27.5%) had ECD. The model with the largest AUC (0.98) was: $\beta = 0.04 * (\text{systolic blood pressure after 1 hour from admission (mmHg)}) + 0.17 * (IVHV (mL)) + 0.87 * (\text{dislocation of transparent partition of the brain (mm)}) - 15.94$ (fig.1). Percent Concordant=94.8. The cut-off value of $\beta > -1.06$ predicts ECD with sensitivity=87.5% and specificity=95.2%.

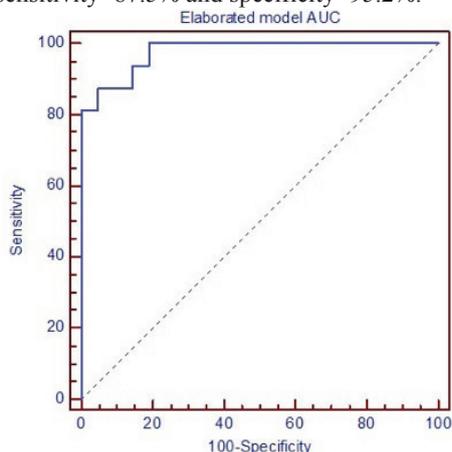


Fig. 1. Elaborated model AUC.

Conclusion: Elaborated prognostic model might be a powerful tool for predicting ECD in acute period of ASSICH and secondary IVH and improving efficacy of treatment.

Disclosure: Nothing to disclose

EP2041

New multivariate prognostic model for predicting early lethal outcome after acute period of spontaneous supratentorial intracerebral hemorrhage with secondary intraventricular hemorrhage

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Background and aims: Identification of vital prognosis in patients with acute spontaneous supratentorial intracerebral hemorrhage (ASSICH) with secondary intraventricular hemorrhage (SIVH) is a very important and relevant in modern angioneurology that can help the practitioners to improve treatment approaches. Therefore the aim was elaboration of new multivariate statistical for predicting ELO after ASSICH with SIVH using clinical and paraclinical parameters.

Methods: 69 patients (mean age 64.4 ± 1.5 years) were studied during the acute period of disease. Clinical examination included evaluation by National Institute of Health Stroke Scale (NIHSS), Glasgow Coma Scale (GCS), Full Outline of UnResponsiveness score (FOUR). Severity of SIVH was verified by the different scores: IVH, Hemphill-ICH, mICH-A, mICH-B, ICH-GS using clinical parameters and parameters of computer tomography. Intracerebral hemorrhage volume (ICHV) and secondary IVH volume (IVHV) were calculated by formulas: $ICHV = (a * b * c) / 2$ and $IVHV (mL) = e^{(IVHS \text{ score}/5)}$. Elaboration of prognostic model was made by logistic regression and ROC-analysis.

Results: Out of 69 stroke patients, 13 (18.8%) had died. The model with the largest AUC was: $\beta = -0.09 * \text{age (years)} + 0.17 * (\text{NIHSS score at admission}) + 0.13 * (IVHV (mL)) - 1.37$. Percent Concordant=95.6. Elaborated model characterized by higher AUC (0.99) (fig. 1), than used in routine clinical practice standard scores: Hemphill-ICH (0.74), mICH-A (0.81), mICH-B (0.74) and ICH-GS (0.60). The cut-off value of $\beta > -2.18$ predicts ELO with sensitivity=91.7% and specificity=92.9%.

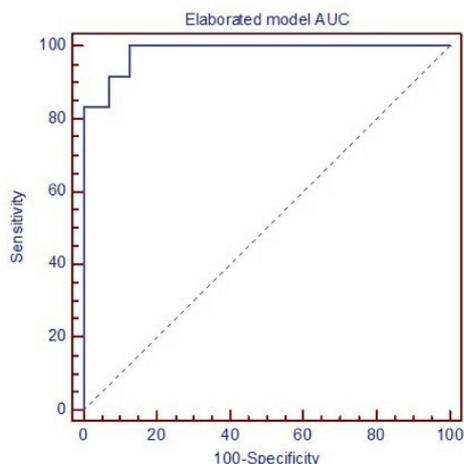


Fig. 1. Elaborated model AUC.

Conclusion: Elaborated prognostic model might be a powerful tool for predicting ELO in ASSICH with SIVH and improving efficacy of treatment.

Disclosure: Nothing to disclose

EP2042

Cancelled

EP2043

Stuttering as stroke presentation

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Background and aims: Acquired stuttering is a rare and poorly understood condition, the majority being of ischemic etiology. It has been described in both dominant and non-dominant hemispheric lesions and in all lobes except the occipital.

Methods: We describe a case of an acquired stuttering as stroke presentation.

Results: 38-year-old right-handed woman, recently diagnosed with hypertension, without history of development stuttering, presented in our hospital with sudden and recurrent episodes of speaking difficulty, with progressive worsening in the past two weeks. Repetitions and prolongations were noted, occurring on grammatical as well as on substantive words, in all positions of the words in the sentence, consistent across every speech tasks (reading, singing), and rarely paraphasias. The remaining neurological examination was unremarkable, except for mild attention deficit. Brain CT was described as normal. Electrocardiogram was unremarkable. Cervical and transcranial ultrasound was compatible with distal middle cerebral artery occlusion. Blood and cerebrospinal fluid investigations were normal, as well as the echocardiogram. Cerebral MRI and MR angiography revealed an acute ischemic lesion affecting the left fronto-parieto-temporo-occipital cortex and lenticulocapsular region, terminal internal carotid and anterior cerebral arteries stenosis, and middle cerebral artery occlusion. Conventional angiography confirmed the previous described and showed evidence of collateral circulation, compatible with a unilateral moyamoya pattern.

Conclusion: We describe a case of a large ischemic lesion presenting only with acute stuttering and rare paraphasias, with the further investigation revealing a moyamoya syndrome. Although frequently attributed to functional disturbances, we emphasize the need to investigate a structural cause in acquired stuttering.

Disclosure: Nothing to disclose

EP2044

Cancelled

EP2045

Cancelled

EP2046

Cancelled

EP2047

Cancelled

EP2048

Cancelled

EP2049

Cancelled

EP2050

Predictors of 3-months functional outcome in nontraumatic intracerebral hemorrhage

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Background and aims: Outcome in patients with intracerebral hemorrhage (ICH) is commonly predicted as 30-day mortality. There are less data concerning factors affecting the long-term and functional outcome. The aim of our study was to determine the prognostic value of ICH baseline parameters for 3-month functional outcome of ICH.

Methods: 89 patients with nontraumatic ICH were included in the study. Evaluated parameters were age, neurological status characterized by National Institute of Health Stroke Scale (NIHSS), hematoma volume measured using 3D Slicer, presence of intraventricular hemorrhage (IVH) and hematoma location categorized as lobar, deep brain (including basal ganglia and thalamus), brainstem and cerebellar. The outcome of interest was 3-months functional outcome classified as good (modified Rankin Scale (mRS) 0-2) and poor (mRS 3-6).

Results: A binomial logistic regression was performed. Of the imputed variables were only NIHSS and age statistically significant. Increasing age and NIHSS score were associated with poor outcome. HR for poor outcome was 1.284 (95% CI 1.159-1.422, $p < 0.001$) for NIHSS and 1.055 (95% CI 1.026-1.084, $p < 0.001$) for age.

Conclusion: Age and the severity of neurological deficit are the crucial baseline parameters for predicting 3-months functional outcome in patients with nontraumatic ICH.

Disclosure: Nothing to disclose

EP2051

Decompressive craniectomy in middle cerebral artery malignant ischemic stroke: 11 years of experience

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Background and aims: Middle cerebral artery (MCA) ischemic stroke has high morbidity and mortality related to cytotoxic edema mass effect. RCT favored better functional and mortality outcome with decompressive craniectomy (DC) in a selected group of patients. We describe the experience of our center.

Methods: Retrospective analysis of clinical charts from every patient with MCA ischemic stroke who underwent DC at our center from January/2006 to October/2016.

Results: Thirty-seven patients were included (average 49 yo): 57% with DC until 48h of symptoms. At 12 months, mRS distribution was: 1 - 2.9%; 2 - 5.7%, 3 - 22.9%, 4 - 40%, 5 - 5.7%, 6 - 22.9%. The 31% who could walk unassisted were younger (40 vs. 53, $p=0.034$) and had lower GCS score at admission (11±3 vs. 13±2, $p=0.038$). Mortality was lower for those with smaller infarction area at admission (68% of survivors had <1/3 MCA territory vs. 44.4% of those who passed away, $p=0.046$). Only younger age was a positive predictor of $mRS \leq 3$ [OR=1.07 (IC95% 1.003-1.133)]. Prognosis was not different according to time from symptoms to surgery (average 54h) or incidence of surgical complications.

Conclusion: Our DC patients had the prognostic benefit described in previous studies of DC vs. best medical therapy, with lower mortality and 31% walking unassisted at 12mo. Surgical complications did not impact outcome, favoring the safety of the procedure.

Disclosure: Nothing to disclose

EP2052

Genome-wide association study reveals a distinct locus associated with early neurological status after acute ischemic stroke

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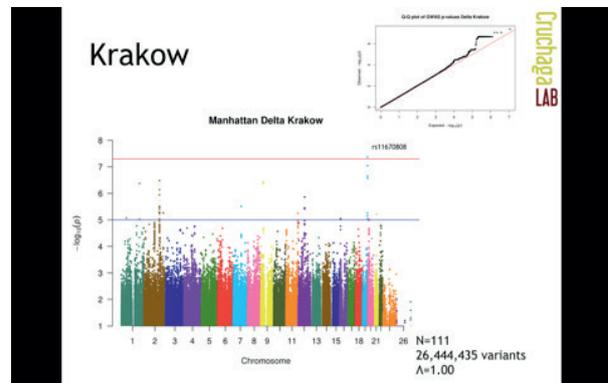
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Introduction: Post-event pathophysiological processes are known to influence neurologic status after acute ischemic stroke (AIS) but it is uncertain if genetic factors affect early outcome.

Hypothesis: Early neurological change after AIS is influenced by genetic variants.

Methods: AIS patients were prospectively enrolled at Jagiellonian University in Krakow, Poland. Early change in neurological status was assessed by NIHSS scores taken within 6 hours of stroke onset, and after 24 hours, using $\Delta\text{NIHSS}_{24\text{h}} = \text{NIHSS}_{6\text{h}} - \text{NIHSS}_{24\text{h}}$. Genotyping was generated for common variants, imputing up to 4 million SNPs. A GWAS was performed using the model: $\Delta\text{NIHSS}_{24\text{h}} = \Delta\text{NIHSS}_{6\text{h}} - \text{NIHSS}_{24\text{h}}$, age, sex, SNP, PCA1-2. The population was analyzed through overall statistical analysis taking into account population mixing (MANTRA).

Results: 111 patients (ages 32-95, 47% female) were found to have an NIHSS_{6h} score of 6 (IQR 10) and $\Delta\text{NIHSS}_{24\text{h}}$ score of 2 (SD 5). One novel locus influenced $\Delta\text{NIHSS}_{24\text{h}}$ with genome-wide significance (Figure): rs11670808 in an intron of NLRP11 (chromosome 19) was identified. NLRP11 encodes NLR family pyrin domain containing 11; a part of a subfamily of proteins called NALPs. NALPs are a subset of the CATERPILLAR protein family, a large family of inflammation regulators. NLRP11 is involved in cell signaling by inflammasomes, complexes that activate caspase 1 and in turn pro-inflammatory cytokines IL-18 and IL-1 β .



GWAS for Delta NIHSS

Conclusion: In our population of AIS patients, we found a genetic locus that influences early neurological change after AIS. This gene has been shown to be implicated in inflammatory processes, particularly in activation of pro-inflammatory cytokines. Replication in an independent cohort is ongoing.

Disclosure: This study is funded by a grant from the NIH, and also a training grant from the American Heart Association/American Stroke Association.

Clinical neurophysiology

EP2053

Neurophysiological characteristics of restless legs syndrome in Parkinson's disease

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Background and aims: Restless legs syndrome (RLS) in patients with Parkinson's disease (PD) occurs more frequently than in general population. It is caused by hypofunction of diencephalic-spinal dopaminergic tracts leading to changes in excitability of the spinal segmental apparatus with development of sensory-motor disorders.

Aim: To investigate the neurophysiological features of RLS in PD.

Methods: We investigated somatosensory evoked potentials (SEPs), blink reflex (BR) and sympathetic skin response (SSR). 82 patients with PD aged 40-70 years were examined: 36 with RLS (1st group) and 46 -without RLS (2nd group). 30 healthy individuals were included in the control group.

Results: SEPs study revealed that in the 1st group, the interpeak intervals (IPI) N9-N13, N11-N13 were significantly shorter and the IPI N13-N20 was longer as compared with 2nd group. A significant increase in the amplitudes N20-P23 and N13-P18 was also revealed in the 1st group, which reflects sensitization processes in patients with RLS. SSR study revealed prolonged latent period and an increase in the peak amplitude in the 1st group and positive correlation between the severity of RLS (according to International RLS Severity Scale) and SSR latency. Trend to hyperexcitability answers of BR was observed, which reflects insufficiency of the inhibitory mechanisms at the segmental level and deficiency of suprasegmental descending control in PD patients with RLS.

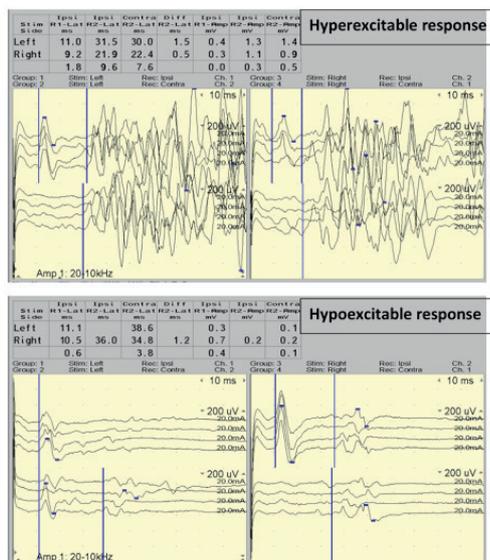


Fig. Examples of the BR registration

Conclusion: A change in the complex interaction between the peripheral, spinal and cerebral divisions of the nervous system was revealed in RLS. Somatosensory disturbances and changes in brainstem and spinal reflexes probably determine the clinical features of RLS in PD.

Disclosure: Nothing to disclose

EP2054

Navigated transcranial magnetic stimulation in differential diagnosis of amyotrophic lateral sclerosis (ALS) and ALS mimic syndromes

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Background and aims: Signs of upper motor neuron involvement are often difficult to elicit in patients with ALS, especially at the early disease stages. The present study aims at investigating diagnostic possibilities of navigated transcranial magnetic stimulation (TMS) in patients with ALS and ALS mimic syndromes.

Methods: A total of 28 patients with pure lower motor neuron syndrome, suspected ALS or possible ALS were recruited into the study. Navigated TMS (NBS eXimia Nexstim) included measurement of resting motor threshold (MT), central motor conduction time (CMCT), cortical silent period (CSP) duration and paired-pulse stimulation with measurement of short-interval intracortical inhibition (SICI) and intracortical facilitation (ICF). Also we mapped cortical representation of musculus abductor pollicis brevis and analyzed the size of muscle representation and the weighted size.

Results: After extensive investigations and clinical follow-up during 6-12 months 9 patients were diagnosed with ALS mimic syndromes (multifocal motor neuropathy, Kennedy's disease, Hirayama's disease), 19 patients were eventually diagnosed with ALS. There was a significant reduction in SICI ($p < 0.001$) and CSP duration ($p < 0.001$) in ALS patients compared to patients with ALS mimic syndromes. The weighted size of muscle representation was significantly smaller in patients with ALS ($p < 0.05$), although the size of muscle representation was not significantly different. There was no significant difference in CMCT, MT and ICF across the groups.

Conclusion: A reduction in SICI and CSP duration (indicative of motor cortex hyperexcitability) and decrease in the weighted size of muscle cortical representations may be considered as diagnostic biomarkers that distinguish ALS from mimic syndromes.

Disclosure: Nothing to disclose

EP2055

Shaky legs: The clinical spectrum and treatment of primary orthostatic tremor; a systematic overview

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Background and aims: Orthostatic tremor (OT) is characterized by a high-frequency tremor of the leg muscles during stance, resulting in an unsteady feeling. Although an increasing number of publications on OT reflect a growing scientific interest in the disorder, pathophysiology is still not understood. Treatment options are limited and often not satisfactory. A systematic literature search on primary OT is lacking the literature.

Methods: Here we review data of a total of 617 primary OT-patients, retrieved after a systematic search in Pubmed (583 individual patients from 45 case reports, 20 case series, and 7 therapeutic trials) and from a questionnaire-based study in Dutch OT-patients (n=34).

Results: Overall, 67% of primary OT patients is female; mean age at onset is 57 (17-81) years. Six percent (22 of 390 cases) has a positive family history for OT. Mean delay to diagnosis is 7.7 years (n=268). A substantial number of patients reports falls. Quality of life is affected. Clonazepam is the most prescribed drug, but is not always effective. Trials report a possible positive effect of gabapentin. Deep brain stimulation (DBS) has shown a positive effect in 6 out of 7 patients.

Conclusion: Primary OT can be disabling and is under-recognized. The most effective treatment remains uncertain, with some evidence for gabapentin and clonazepam. DBS provides an alternative for drug-resistant and disabling OT, although long term effects are still uncertain. Increasing attention for OT will probably shorten the delay in time to diagnosis and possibly lead to development of better treatment options.

Disclosure: Nothing to disclose.

EP2056

Cancelled

EP2057

Somatosensory evoked potentials (median SEP) in multiple sclerosis: Influence of montage on latency, amplitude and central conduction time and implication for multicentre trials

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Background and aims: To determine comparability of two recommended recording montages of median somatosensory evoked potentials (SEP), as SEP are part of multimodal EP which may become an outcome measure in multicentre clinical trials.

Methods: 81 patients with relapsing multiple sclerosis (MS) (mean age: 37.5y, median EDSS: 2.0) and 49 healthy controls (HC) had median SEP recordings with high-resolution EEG. Two standard montages were extracted: M1 (C3'/C4'-Fz, C7-Fz) and M2 (C3'/C4'-C4'/C3', C7-EP contralateral). N20 and N13 latency, N20-P25 amplitude and central conduction time (CCT) were independently evaluated by two neurophysiologists (VB, MH) blinded to diagnosis using EPMark. Nine artifactual curves (4%) were excluded.

Results: To determine the physiological effect of montages and not the effect of uncertainty in rating, 12 curves (5%) with a N20-latency difference >2 msec between montages were excluded. In HC, N20 and N13 latencies in M1 were significantly (p<0.05) longer than in M2 (mean difference: 0.17 and 0.39msec). In MS patients, only N20 latency differed (0.21msec). Differences in CCT (HC: 0.19, MS: 0.21 msec) were not significant. Amplitudes were 40% and 41% smaller in M2 compared to M1 (p<0.001).

Conclusion: N20-latency is significantly later in Fz-compared to ipsilateral C'-reference independent of group, most likely due to injection of a frontal positivity. This difference is 2-6x smaller than variability in HC and thus clinically not relevant. The much higher amplitude favours Fz-reference. However, in clinical trials both montages may be employed in parallel as the technicians' routine is important in achieving standardized follow-up assessments.

Disclosure: VB received a travel grant from the European Academy of Neurology (EAN). The study was supported by the Swiss National Science Foundation (SNF; grants 33CM30-140338 and 326030_128775).

EP2058

Cancelled

EP2059

Small fiber neuropathy in neurological diseases: Contribution of laser-evoked potentials

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Background and aims: Many studies documented the presence of small fiber neuropathy (SFN) in different neurological diseases, such as Amyotrophic lateral sclerosis (ALS) and Fabry disease (FD). Laser-evoked potentials (LEPs) are an emerging neurophysiologic technique to evaluate small fiber involvement, even if no clear data are available concerning their sensitivity, compared to skin biopsy.

Methods: We recruited 34 patients (age 56.2±13.2): 10 ALS patients (5 M, 5 F), 10 FD patients (10 F) and 14 patients with diagnosis of acquired small fiber neuropathy (6 M, 8 F), in order to evaluate LEPs sensitivity. All patients had previously undergone skin biopsy (from thigh and lower leg, using a 3mm punch), disclosing decreased epidermal nerve fiber density. LEPs were carried out using a Nd-YAP laser (1340nm) by stimulating hand, foot and face skin surface.

Results: 74% of patients showed abnormalities of LEPs, respectively 80% in ALS, 60% in FD and 79% in other SFN, with absent LEPs (40%), decreased amplitude (33%), increased latencies (20%) or both (7%). Comparing face, hand and foot, A- δ LEPs were more often abnormal recording from foot (41%). Interestingly, C fibers in the trigeminal territory showed the highest abnormalities (50% of patients).

Conclusion: LEPs showed a good sensitivity in evaluating SFN. Our findings of a higher involvement of C fibers rather than A- δ in SFN deserve a better characterization. However, this study needs to be extended to a larger number of patients, before drawing any definite conclusion.

Disclosure: Nothing to disclose

EP2060

Electromyographic study of thoracic paraspinal and rectus abdominis muscles in the diagnosis of ALS

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Background and aims: The diagnosis of definite Amyotrophic lateral Sclerosis (ALS) requires the presence of upper and lower motor neuron involvement in three spinal regions. The aim of this study was the comparison of active denervation (fibrillation and/or positive sharp wave potentials) in Thoracic paraspinal muscles (T- PMS) with those in Rectus abdominis (RA) in patients with definite ALS.

Methods: Needle electromyographic study (EMG) with concentric needle electrode was performed in T-PSM at T8-T10 level and in RA of 95 patients with ALS.

Results: 95 patients with definite ALS were investigated, 50 men and 45 women, of median age 61.2 yrs (30-83). Active denervation was found more frequently in T-PSM than in the RA (80% vs 65%, p<0.05). Increasing age was related to more severe denervation in the RA (p<0.01). Duration of symptoms, Creatine Kinase levels, sex, initial symptoms (upper limb, lower limb or bulbar), degree of denervation and Revised ALS Functional Rating Scale score were not associated with RA and T-PSM denervation.

Conclusion: T-PMS EMG is recommended for the detection of active denervation in patients with ALS. In case of normal EMG in RA, T- PSM must also be tested. On the contrary, absence of active denervation in T-PSM is rarely associated with active denervation in RA.

Disclosure: Nothing to disclose

EP2061

Cancelled

EP2062

Segmental contact heat-evoked potentials in healthy controls and diabetic polyneuropathy patients

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Background and aims: Contact heat-evoked potentials (CHEPs) provide a means of assessing functional impairment of small nerve fibres and the spinothalamic pathway. The aim of this study was to investigate the impact of physiological and test variables on CHEPs latency and amplitude parameters, and to determine the applicability of the method for diabetic neuropathy (DN) patients.

Methods: In 30 DN patients and 70 healthy subjects, standard CHEPs were tested at wrist and ankle (C6, C8, L4 and L5 dermatomes) using two algorithms: “basic” with temperatures ranging from 35° to 50°C and “intensive” from 42° to 52°C). Latencies and amplitudes of N2/P2 response, together with tolerability of the thermal stimuli were (semi-quantitatively) evaluated.

Results: CHEPs were largely well-tolerated and responses could be evoked in most of the individuals tested. Latencies were shorter and amplitudes higher at the wrist compared to the ankle, as they were when applying the intensive algorithm compared to the basic one. The differences between the C6 and C8 dermatomes (as well as between L4 and L5) were not significant. Amplitudes decreased with age, while latencies increased slightly with age and height. At group level, reduction of amplitudes constituted the major difference between healthy controls and DN patients.

Conclusion: CHEPs are an efficient and well-tolerated method of functional testing of pain-related tracts both in healthy controls and DN patients. Age, height, testing algorithm and the area tested need to be considered in the interpretation of the results. Reduction of amplitudes appears to be the most prominent abnormality in DN patients.

Disclosure: Nothing to disclose

EP2063

Tibial somatosensory evoked potentials predict walking speed in early multiple sclerosis

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Background and aims: We aimed to evaluate somatosensory evoked potentials of the tibial nerve (SSEPt) in correlation with timed 25 foot walk test (T25FW) and MRI findings in patients with first symptom of multiple sclerosis (MS).

Methods: In 120 MS patients (mean age 32.2±8.7 years, 84 females), EDSS, T25FW, brain and spinal cord MRI and SSEPt were performed. P40 latencies and N22a-P40 interlatency were analyzed and zscore for each latency was calculated and combined into SSEPt zscore. MRI was analyzed for the presence of brainstem and cervical spinal cord lesions.

Results: Walking speed measured with T25FW significantly correlated with SSEPt zscore ($r_s=0.211$; $p=0.021$). When looking each component of the SSEPt separately, T25FW significantly correlated with left P40 wave latencies ($r_s=0.223$; $p=0.014$) and N22a-P40 interlatencies ($r_s=0.241$; $p=0.008$). There were no significant correlations for other SSEPt parameters. Furthermore, patients who presented with transverse myelitis ($N=41$) and patients who had spinal cord lesions on the MRI had significantly higher SSEPt zscore compared to other patients (0.07 vs. -0.28, $p=0.019$ and -0.02 vs -0.38 $p=0.023$; respectively). A linear regression was calculated to predict T25FW based on SSEPt zscore, age, gender and cervical spinal cord MRI lesions. Significant regression equation was found ($F(4,87)=6.815$, $p<0.001$), with an $R^2=0.239$. SSEPt zscore corrected for age, gender and cervical spinal cord MRI lesions is statistically significant predictor for T25FW ($B=0.268$, $p=0.023$).

Conclusion: In MS patients SSEPt is a potential marker of walking speed and indicates presence of functional impairment at the level of the spinal cord.

Disclosure: Funding: Croatian Science Foundation grant HRZZ UIP-11-2013-2622

EP2064

Sensory fibers in Martin-Gruber anastomosis: An electrophysiological study

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Background and aims: Anatomical variations in the innervations of intrinsic hand muscle are well known as Martin-Gruber anastomosis (MGA), spread from the median to the ulnar nerves in the forearm. This anastomosis predominantly consists of motor axons, with rare sensory contribution. Although anatomical studies have shown that a crossover of sensory fibers is not rare in Martin-Gruber median-ulnar anastomosis, it has been electrophysiologically described only in rare subjects. The aim of our study was to investigate the frequency of sensory fibers in MGA.

Methods: In order to demonstrate the presence of sensory fibers in MGA, we stimulated the median nerve at the elbow and recorded the antidromic sensory potential from ulnar innervated digit (5th finger), using surface electrodes.

Results: A total of 113 arms were analyzed with presence of motor MGA. Sensory MGA were present in 35 arms (30.9%). There were 59 left hands with motor MGA, of which 15 (25.4%) were with sensory MGA, and 54 right hands with motor MGA, and 20 (37%) of them had sensory MGA. There was no a significant difference between the presence of sensory fibers depending on the right or left hand ($p=0.56$), or the sex ($p=0.49$).

Conclusion: The presence of sensory fibers in MGA median-ulnar anastomosis by electrophysiological study is not rare. Knowledge of the anatomical variations relating to the innervation of the hand has great importance, especially with regard to physical examination, diagnosis, prognosis and surgical treatment.

Disclosure: Nothing to disclose

EP2065

Self-rated health and sense of coherence in multiple sclerosis patients

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Background and aims: Multiple sclerosis (MS) is a chronic disease with psychosocial ramifications. Sense of coherence (SOC) refers to the extent to which life is perceived as comprehensible, manageable, and meaningful. It might play role in self-rated health (SRH), which lowly scored, predicts poor health outcomes. The aim of this study was to examine the association between SOC and SRH in MS patients.

Methods: 134 patients completed a socio-demographic questionnaire, the first item of the Short Form-36 Health Survey, and Short form-13 Orientation to Life Questionnaire. Physical disability was assessed using Expanded Disability Status Scale. SRH was dichotomized into poor health- and good health- group (cutoff score 25). T-test and chi-squared test were used to estimate the differences between the groups. Logistic regression was performed to investigate the effect of SOC on SRH when adjusting for sociodemographic and clinical variables.

Results: The good SRH patients were younger ($p < 0.001$), with relapsing-remitting MS ($p < 0.001$), less disabled ($p < 0.001$), with higher SOC ($p=0.002$), employed ($p=0.002$), and on immunotherapy ($p=0.01$). The logistic regression analysis showed that, after adjusting for other variables, an incremental change of SOC by one unit, increases the odds of reporting good SRH by 10.5% (Odds Ratio 1.05; 95% Confidence Interval 1.02-1.09).

Conclusion: This study shows the positive effect of higher SOC on perceived health in MS patients. Strategies oriented to enhance SOC may promote health and reduce poor outcomes.

Disclosure: Nothing to disclose

EP2066

A neurophysiological study of small-diameter nerve fibers in the hands of hemodialysis patients

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Background and aims: The prevalence of uremic polyneuropathy varies between 60 and 100% and remains a major disabling feature in the life of uremic patients. The aim of the present study was to evaluate the function of small-diameter A-delta nerve fibers, in the hands of hemodialysis patients.

Methods: A total of 38 randomly selected patients treated three times weekly with hemodialysis were evaluated. The control group consisted of 38 age-matched healthy subjects. The mean age of hemodialysis patients and healthy subjects did not differ significantly.

The function of A-delta nerve fibers was measured by cutaneous silent period (CSP). CSP was elicited by nociceptive electrical square pulse stimulation using bipolar electrodes at the palmar distal tip of digit II, stimulating median nerve fibers. Recording electrodes were placed over thenar muscles in the standard the position as for median nerve motor conduction study. CSP onset and end latency, and the difference between the two latencies – duration of CSP (muscle activity suppression), were calculated.

Results: The mean CSP onset latency in hemodialysis patients with and without arteriovenous fistula was markedly longer compared with the control group ($p < 0.0001$). The same relationship was found for CSP end latencies. CSP duration did not demonstrate any difference between the two groups. CSP onset latency was observed in 12/38 (32%) hemodialysis patients.

Conclusion: The evaluation of CSP is a useful method for detecting the function of A-delta fibers. The delayed CSP onset latency observed in 1/3 of hemodialysis patients reflects the impairment of the afferent conduction of A-delta fibers.

Disclosure: Nothing to disclose

Cognitive neurology/neuropsychology 2

EP2067

A descriptive analysis of behavioural and psychological symptoms in logopenic variant of primary progressive aphasia

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Background and aims: The logopenic variant of primary progressive aphasia (lvPPA) is a distinctive variant of PPA, in which recent evidence shows that Alzheimer disease (AD) might be the most common underlying pathology. Our goal is to evaluate the frequency of behavioural and psychological symptoms (BPS) in lvPPA.

Methods: This is a descriptive study that prospectively recorded data of 20 consecutive patients who met lvPPA criteria: word retrieval and sentence repetition deficits, phonologic paraphasias, sparing of single word comprehension and motor speech, absence of frank agrammatism and predominant left posterior perisylvian or parietal atrophy on MRI and/or hypoperfusion or hypometabolism on SPECT or PET (Gorno-Tempini ML et al, 2011) at the Hospital Universitario de Salamanca, Spain (mean age at onset 73.1±4.9 years, mean duration of dementia 3.8±2.3 years, 55% women). The Neuropsychiatric Inventory (NPI) was used to assess BPS.

Results: At least one BPS occurred in 100% of lvPPA participants, the median NPI score was 34 (range:10-86), with a median number of 5 symptoms per patient. The most frequent symptoms were anxiety (80%), depression (70%), apathy (70%) and sleep disturbances (60%), followed by agitation (50%), disinhibition (50%), appetite/eating abnormalities (45%), irritability (40%), aberrant motor behaviour (40%), hallucinations (35%), delusions (25%) and euphoria (10%). It is remarkable that 7 of 9 patients with appetite/eating abnormalities showed hyperphagia.

Conclusion: BPS are frequent in lvPPA. New investigations are required to better evaluate the relationship between histopathologic evidence of specific neurodegenerative pathologies in lvPPA (e.g. AD, frontotemporal lobar degeneration [FTLD]-TDP, other) and different BPS profiles.

Disclosure: Nothing to disclose

EP1046

Complex visuo-constructive deficits in subjective memory complaint: A combined quantitative and qualitative study

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Background and aims: Subjective Memory Complaint (SMC) is a possible prodrome of Alzheimer's disease (AD) dementia. Objective impairments in SMC may be revealed by in-depth neuropsychological evaluations. Hereby, we analysed in SMC subjects complex visuo-constructive performances and their relationship with basic cognitive functioning in order to detect subtle impairments and possible correlation with working memory and executive performances.

Methods: Thirty-seven SMC subjects (10 male; age=67.27±5.53 years; education=12.86±3.29) were enrolled. All participants completed a detailed neuropsychological battery. A combined quantitative and qualitative scoring approach was used to analyse Clock Drawing Test (CDT) and Rey-Osterrieth Complex Figure (ROCF) performances. Correlations between CDT/ROCF and other cognitive scores were explored.

Results: Twenty-five subjects presented with a subjective memory disorder (i.e., no objective cognitive deficit), while 12 subjects showed objective impairments at memory, executive and/or visuo-constructive tasks. Statistical analyses highlighted significant correlations between the number of "omitted elements" at both CDT and ROCF tasks and working memory abilities (i.e., Digit Span backward). Additionally, the number of "distortion" (i.e., element incomplete but placed properly) at the ROCF task was correlated with attentional/executive (i.e., Trial Making Test B) performances.

Conclusion: In this study, we provided evidence in SMC subjects of impairments at non-memory tasks including complex visuo-constructive tests. These were crucially affected by working memory and attentional/planning deficits. Our results suggest the importance of a careful cognitive assessment of non-memory domains in case of SMC in order to obtain a better diagnosis and make prediction of the possible evolution.

Disclosure: Nothing to disclose

EP2068

Brain wave entrainment using alpha frequency binaural beats on adolescent swimmers

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Background and aims: Binaural beats combined with music therapy and mental training skills were more effective in increasing α waves was suggested to improve anxiety in swimmers.

Aim: The effect of brain wave entrainment in swimmers using binaural beats set at alpha range was investigated. EEG and reaction time were measured before and after sessions of relaxation techniques, music therapy and mental training with and without binaural beats.

Methods: 11 adolescent elite swimmers (4 females, 7 males) were subjected to 18 sessions of mental training skills including relaxation techniques, positive thinking and imagery. 7 swimmers were randomly assigned to group I and received sessions of binaural beats and music therapy and the other 4 to group II receiving just music therapy. (both groups were blind to the music type) EEG and reaction time was measured pre and post the sessions. A written consent was taken from the parents prior to the study.

Results: There was a significant EEG waves change during the relaxation time ($p=0.05$) and positive thinking phase ($p=0.05$). The EEG frequencies significantly decreased (both qualitatively and quantitatively) in swimmers included in group I (with the beats) than those in group II. In addition to this statistically significant improvement in the reaction time in their performances observed in group I, which was significantly shorter ($p=0.01$) compared to group II.

Conclusion: Relaxation techniques and binaural beats added to music may have a positive effect on athletic performance of swimmers

Disclosure: Nothing to disclose

EP2069

Cancelled

EP2070

Motor aspects of daily living are inversely associated with anxiety and dysphoria in Parkinson's disease dementia but not in dementia with Lewy bodies

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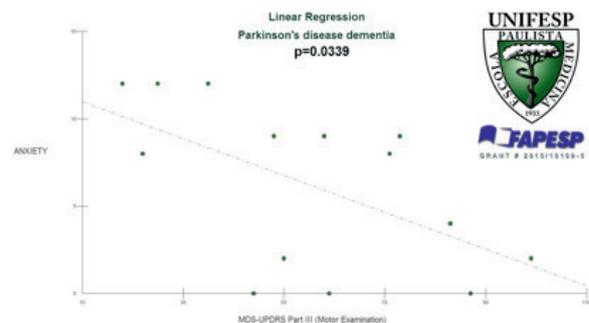
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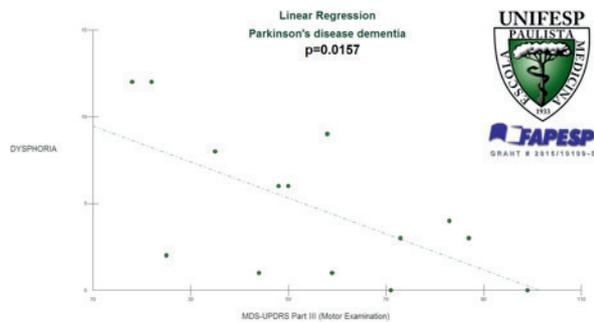
Background and aims: Lewy body dementia syndromes present motor impairment and neuropsychiatric symptoms among their main manifestations. It is unclear how motor experiences are associated with behaviour in these patients.

Methods: Participants with Parkinson's disease dementia (PDD) or dementia with Lewy bodies (DLB) were screened with the Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) and the 12-item Neuropsychiatric Inventory. All tests were correlated with each other by way of linear regressions, significance at $p < 0.05$.

Results: We included 50 patients - 14 patients with PDD (28.0%) and 36 patients with DLB (72.0%); 23 (46.0%) had mild dementia, 17 (34.0%) had moderate dementia, and 10 (20.0%) had severe dementia; 21 (42.0%) used Levodopa (12 with PDD, 9 with DLB), 34 (68.0%) used cholinesterase inhibitors (9 with PDD, 25 with DLB), 25 (50.0%) used anti-depressants (9 with PDD, 16 with DLB), and 24 (48.0%) used anti-psychotics (6 with PDD, 18 with DLB). For PDD, MDS-UPDRS Part II (Motor Experiences) was inversely associated with anxiety ($p=0.0372$) and dysphoria ($p=0.0162$) total scores, but not with other symptoms ($p > 0.07$). Also for PDD, MDS-UPDRS Part III (Motor Examination) was inversely associated with anxiety ($p=0.0339$) and dysphoria ($p=0.0157$) total scores, but not with other symptoms ($p > 0.07$). No behavioural symptoms were associated with MDS-UPDRS scores for patients with DLB ($p > 0.10$).



Association of anxiety scores with MDS-UPDRS Part III in Parkinson's disease dementia.



Association of dysphoria scores with MDS-UPDRS Part III in Parkinson's disease dementia.

Conclusion: Anxiety and dysphoria usually occur when motor signs and symptoms involved in experiences of daily living are less burdensome in PDD, but not in DLB.

Disclosure: Supported by grant #2015/10109-5, The State of São Paulo Research Foundation (FAPESP).

EP2071

Foreign accent syndrome: Functional or structural cause?

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Background and aims: Foreign accent syndrome (FAS) is a rare motor speech disorder where the affected person speaks in an accent different from their mother tongue. FAS may be organic, with or without structural lesions, or functional and the distinction might be difficult.

Methods: We report two similar FAS cases with presumed different etiologies.

Results: A 27-year-old Portuguese woman presented with an acute motor aphasia and right motor deficit secondary to a left M1 occlusion. She was treated with thrombectomy, maintaining distal M2/M3 occlusion. After the procedure, she gradually recovered all deficits. Her speech was normal beside presenting a foreign spanish accent. The patient had recently started having spanish lessons. Head-CT after 24 hours revealed a left insular and lenticular/capsular infarction. The foreign accent spontaneously resolved after a week. A 36-year-old Portuguese woman presented with a facial asymmetry mimicking a left peripheral facial nerve palsy after spending a week at London. She gradually developed a left motor deficit with gait impairment, visual symptoms and started talking with a foreign accent perceived as english. She also presented a left hand postural tremor that disappeared with distraction maneuvers. Brain MRI and CSF study was normal. Assuming a functional cause, she started sertraline, speech therapy and psychotherapy with partial improvement. During follow-up she had a normal speech for a year while on homeopathic medications. Recently she reappeared at consultation with a minor foreign accent, evident when on stressful situations.

Conclusion: These two cases highlight different features of functional and organic causes of foreign accent syndrome and possible treatment approaches.

Disclosure: Nothing to disclose

EP2072

Cancelled

EP2073

Neuropsychological disorders in early Parkinson's disease and vascular parkinsonism: Experience in Kyrgyz Republic

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Background and aims: Neuropsychological disorders accompany Parkinson disease (PD) and Vascular Parkinsonism (VP) on every stage of development, in clinical semiology, causing a great impact on patients' life-quality.

Objective: investigate existence and evidence of neuropsychological disorders in PD and VP patients.

Methods: 31 patients were studied (18 females, 13 males), where 23 suffered from PD, and 8 – VP. Average age – 64.42 ± 1.1 , disease severity Hoehn and Yahr average stage – 2.5 ± 0.8 . Patients were studied by clinical, bedside examination, somatic and neurological status check, global cognitive function: Mini-Mental State Examination and Montreal Cognitive Assessment (MMSE and MoCA), Zung Self-Rating Depression scale, and Spielberger anxiety scale; instrumental examination (ECG, brain MRI). Statistical analysis is done by SPSS.

Results: Average depression level – 52.7 ± 7.3 of all patients: mild and moderate depression in 82.6% with PD, and 37.5% with VP. 64.5% of all patients suffered increased level of anxiety: PD 78.2%, VP 25%. Cognitive disorders analysis (MMSE, MoCA): mild and moderate cognitive disorders in 30.4% of PD, when 75% of VP patients had moderate and severe cognitive disorders. 64.5% of all patients suffered sleep disorders, insomnia and daytime sleepiness: PD 82.6% and VP 37.5%.

Conclusion: Severe cognitive disorders were observed in Vascular Parkinsonism more often, while mild cognitive disorders were observed in patients with Parkinson Disease. Neuropsychological disorders such as depression, anxiety, and sleep disorders are more frequent in PD patients, though still observed in VP, which suggests a common development mechanism for these disorders.

Disclosure: Nothing to disclose

EP2074

Neuropsychological assessment in initial Hoehn and Yahr clinical stages of Parkinson's disease

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Background and aims: To compare cognitive performances in newly diagnosed patients with Parkinson's disease (PD) at Hoehn and Yahr (HY) stage I or stage II at their first medical evaluation.

Methods: Forty-four drug-naïve patients with newly diagnosed PD at HY Stage I and 40 patients at HY Stage II, matched for all variables but UPDRS total score and its sub-scores, completed a standardized neuropsychological battery. A one-way multivariate analysis of variance (MANOVA) was used to compare cognitive scores of the groups, complemented by Bonferroni corrected univariate analysis of variances (ANOVA). Finally, the prevalence of mild cognitive impairment (MCI) was estimated for patients classified in HY stage I or II.

Results: A general significant difference was found between patients at HY stage I or stage II on neuropsychological performances ($\eta^2 = .645$, $F(16, 67) = 2.31$, $p = .009$), with patients at HY stage I showing higher scores than patients at stage II. Moreover, univariate ANOVAs revealed significant differences between HY stages on Rey's auditory verbal learning test-immediate recall ($p < .0001$), prose recall test ($p < .002$), 10 points Clock Drawing Test ($p < .002$), and, Rey-Osterrieth Complex Figure Test-copy ($p < .002$). PD-MCI occurred in 5 of 44 (11.36%) patients in the HY stage I, and in 15 of 39 (38.46%) patients in the HY stage II.

Conclusion: In drug-naïve, newly diagnosed PD patients, motor disability is associated with cognitive deterioration and higher rate of prevalence of mild cognitive impairment at the first medical evaluation (HY stage).

Disclosure: Nothing to disclose

EP2075

Primary progressive aphasia: A case study

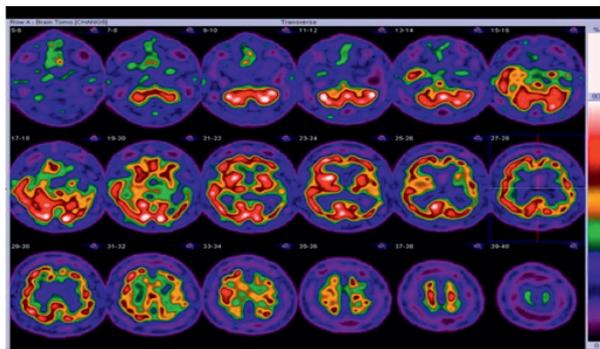
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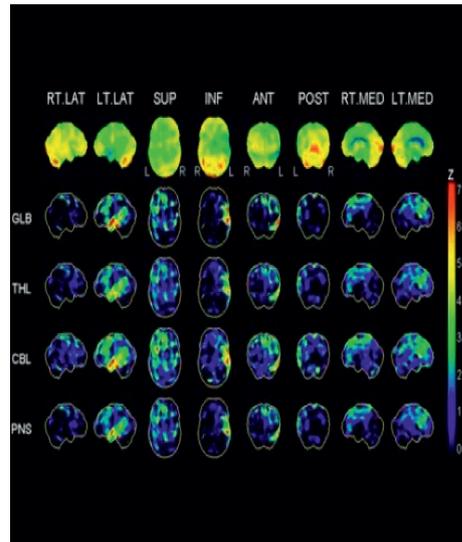
Background and aims: Primary Progressive Aphasia (PPA) is a selective and progressive form of neurodegenerative disease characterized by declining language function. The disease starts with word-finding disturbances (anomia) and frequently proceeds to impair the grammatical structure (syntax) and comprehension (semantics) of language. The clinicopathological correlations in PPA emphasize the contributory role of dementia with Pick's bodies, other tauopathies, and TDP-43 proteinopathies. PPA affects five general linguistic skills: oral and written naming, reading, repetition and general comprehension. Standardized language testing and Neuroimaging is important to diagnose and follow the course of the disease.

Methods: A 83-year-old Caucasian right-handed male first presented in July 2005 with progressive speech difficulty for 4 years. We followed-up the patient over the course of 9 years in the Memory Clinic with Neuropsychological evaluation and radiological imaging. His recent visit demonstrated progressive deterioration of speech and language function with intact comprehension. Neuropsychological evaluation demonstrates Expressive aphasia without paraphasias or comprehension problems. He possesses Normal naming capabilities but abnormal repetition.

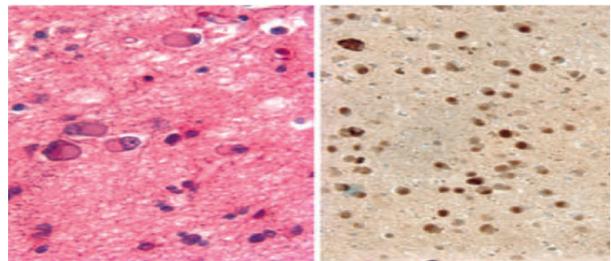
Results: SPECT Perfusion studies show severe perfusion reduction in the left temporal lobe with mild perfusion reduction extending into the left frontal and parietal cortex. Right temporal lobe perfusion uninvolved. Posterior cingulate perfusion preserved



SPECT Perfusion study



SPECT Perfusion study



Presence of Pick bodies on immunohistochemistry

Conclusion: Approximately 10 percent of dementias present as primary progressive aphasia. The disease is progressive and unfortunately, no precise treatment modality is present to halt the progression. Speech and occupational therapy is the mainstay of management. High-frequency repetitive Transcranial Magnetic Stimulation (hf-rTMS), applied to the left prefrontal cortex, may improve the linguistic skills in Primary Progressive Aphasia (PPA).

Disclosure: Nothing to disclose

EP2076

Cognitive dysfunction in six patients with anti-NMDA receptor encephalitis

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Background and aims: Anti-NMDA receptor (anti-NMDAR) encephalitis is a recognized cause of rapid onset encephalopathy with wide phenotypic variability. The clinical presentation includes psychiatric manifestations, memory impairment, seizures, movement disorders, autonomic instability and somnolence. The cognitive profile of these patients is yet to be clarified.

Methods: We performed a retrospective review of clinical and neuropsychological data (Dementia Rating scale-2, DRS-2) of six patients with anti-NMDAR encephalitis followed at Centro Hospitalar do Porto.

Results: Three males and 3 females were included. The first manifestation of the disease occurred between age 8 and 26. None of the patients had an underlying neoplasm. The cerebral MRI had persistent lesions in two patients. Five patients had cognitive evaluations at two different time points (the gap between evaluations varied from 4 months to 4 years). In the acute/subacute phase, one patient scored 135 on DRS-2, while the remainder 4 scored between 63 and 120. Affected domains included attention, language, memory and executive functions. The 4 patients with severe cognitive impairment presented with severe acute psychosis (n=2) and seizures (n=2). Two of these patients were younger than 18 years. In 3/4 patients a follow-up evaluation was performed that showed significant cognitive improvement (DRS-2 125 to 134).

Conclusion: This case series confirms the presence of significant dysfunction in different cognitive domains in the acute/subacute phase of anti-NMDAR autoimmune encephalitis. All patients with follow up evaluation showed substantial cognitive improvement, although some deficits persisted. Cognitive dysfunction was more frequent in patients presenting with psychiatric symptoms or seizures.

Disclosure: Nothing to disclose

EP2077

Possible decline of social cognition in amnesic mild cognitive impairment

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Background and aims: Theory of Mind (ToM) refers to the ability to attribute mental states to other people behavior; it can relate to people feelings (affectiveToM) or intentions (cognitiveToM). Several studies showed an impairment of ToM abilities in neurodegenerative diseases, with conflicting results in patients with Mild Cognitive Impairment (MCI). Our study aims to investigate ToM in MCI.

Methods: We enrolled 36 subjects: 16 with amnesic MCI (aMCI) and 20 healthy controls (HC), matching them for sex, age and educational level. Neuropsychological evaluation included tests to evaluate cognitive status, memory, reasoning, visuo-spatial, attention and executive functions. Two test were used to investigate ToM: the "Reading the Mind in the Eyes" (RME), to evaluate affectiveToM, in which subjects had to guess the emotion or thinking of a person whose eyes are shown in a picture; the "Faux Pas Recognition Test", to evaluate both cognitiveToM and affectiveToM, through the presentation of stories containing faux pas.

Results: In RME we observed lower scores in aMCI than in HC. In the other tests, aMCI showed performances below normal only in memory tasks.

Conclusion: Available data regarding the impairment of ToM in patients with MCI are inconsistent: some studies show a generic dysfunction, rather than a specific deficit of cognitiveToM or affectiveToM; others studies exclude alterations. The results of this study show that a deterioration of affectiveToM is possible in aMCI; this assumption requires further confirmation on a larger sample because it could have important clinical and prognostic implications.

Disclosure: Nothing to disclose

EP2078

Clinico-immunological features patients with limbic encephalites

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Background and aims: Limbic encephalitis (LE) is a heterogeneous group of disorders caused by autoimmunity directed against components of the central nervous system involved in cognition and behavior.

Methods: We present the clinical, immunological, imaging and neurophysiological characteristics of 11 patients that presented to the cognitive neurology clinic with complaints regarding memory impairment and/or behavioral changes and were diagnosed with definite or suspected LE during the years 2012- 2016.

Results: Median age was 57 years (42-69), 100% women. Initial manifestations included subacute cognitive decline (9), seizures (4), depression and behavioral disorders (4). The median MMSE score was 24/30 (range 19-30). Auto antibody seropositivity was depicted in 7 patients. The immunological profile included: VGPC (1), GAD 65 (1), LG1 (1), NMDA (2), anti-Yo and anti Ri (1), anti TPO (2) and anti-amphiphysin (1) antibodies. MRI depicted characteristic findings in 4 patients. Six patients had normal MRI and in one patient a lacunar strokes were depicted. CSF with lymphocytic pleocytosis was found in 4 patients. Eight patients were treated by immunotherapy (IV steroids, plasmapheresis, Imuran). Four patients underwent complete recovery or partial improvement following therapy. The treatment course of one patient was complicated by perforation of the lower esophagus. She eventually died from sepsis. One patient was diagnosed with adenocarcinoma of lung. Her symptomatology resolved following surgery.

Conclusion: LE has to be considered in patients with atypical presentation of cognitive deterioration as early diagnosis and treatment may improve the cognitive outcome. Nevertheless, as the experience with these patients is relatively scarce, treatment should be closely monitored.

Disclosure: Nothing to disclose

EP2079

Cancelled

Epilepsy 2

EP2080

EEG findings in temporal lobe epilepsy and outcome of anterior temporal lobectomy

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Background and aims: To establish if EEG findings are associated with seizure outcomes in patients who undergo anterior temporal lobectomy for temporal lobe epilepsy.

Methods: This was a retrospective data analysis of adult patients who underwent anterior temporal lobectomy at a tertiary neuroscience centre between 2008 and 2015. Demographic and clinical data were collected by review of records. 12 month outcome was categorised based on Engel classification. Fisher exact testing was used to test association between EEG findings and surgical outcomes.

Results: 43 patients were included, with a median age of 41 years (21-63). 22 were female and had left sided lobectomies. 18 (42%) had history of febrile seizures, 41 (95%) had MRI abnormalities, most commonly hippocampal sclerosis (34, 79%). Good (Engel class I) outcome was observed in 29 (69%) patients at 12 months. Videotelemetry was available in 38 (88%) patients. Interictal epileptiform discharges (IED) were present in 35(92%), 25 (71%) of whom had a good outcome; all 3 patients with non specific interictal activity had good outcome ($p=0.55$). 22 of 35 (71%) of those with ipsilateral IED had good outcomes, compared to 3 of 4 with bilateral IED (75%, $p=1.00$). Features of the ictal rhythm including dominant frequency (theta versus delta), lateralisation (ipsilateral versus non lateralised and bilateral), timing (early versus delayed) and localisation (anterior temporal/ sphenoidal versus mid or posterior temporal) did not show significant association with outcomes

Conclusion: In this population of lesional temporal lobe epilepsy, interictal and ictal EEG findings did not show significant association with surgical outcomes.

Disclosure: Nothing to disclose

EP2081

Long term follow-up of recurrent status epilepticus and stroke-like episodes in a MELAS patient.

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Background and aims: Mitochondrial encephalomyopathy, lactic acidosis and stroke-like episodes (MELAS) is a disorder commonly caused by the A3243G/tRNA^{Leu} mutation of mitochondrial DNA (mtDNA). MELAS patients are considered at high risk of epilepsy and status epilepticus (SE) during stroke-like episodes (SLEs). SLEs in MELAS show a predilection for the occipital lobe, which also correlates with the localization of focal epileptic activity on EEG.

Methods: We describe the long-term follow-up of a patient with A3243G/tRNA^{Leu} mutation presenting with recurrent focal SE, mostly occurring during SLEs. Neuroimaging, EEG and SLE treatment are discussed.

Results: This 29-year-old patient carries the mtDNA A3243G/tRNA^{Leu} mutation. The mother died at 40 years during SE associated with SLE. The patient suffered photosensitive epilepsy since 17 years. Since 23 years he presented recurrence of 7 episodes of occipital SE (elementary visual hallucinations, oculo-clonic seizures) with hemianopia mostly associated with lactic acidosis and stroke-like episodes. SE was refractory to iv lorazepam, diazepam, phenytoin and levetiracetam. SE was effectively treated with iv high-dosage Midazolam. In one episode Propofol was used during SE and the patient suffered multiple organ failure (Propofol infusion syndrome-PRIS).

Conclusion: We report a MELAS patient with recurrent occipital SE and SLEs. SE recurred with an increasing frequency over the years. Midazolam infusion is a first-line drug in SE treatment. Based on the occurrence of PRIS in our patient and evidence of mitochondrial toxicity induced by Propofol this drug should be avoided in patients with mitochondrial encephalopathy.

Disclosure: Nothing to disclose

EP2082

Falls in temporal lobe epilepsy

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Background and aims: The main aim of this study was to evaluate the association of sudden, unexpected falls and temporal lobe epilepsy

Methods: We have retrospectively analyzed data of all patients who underwent presurgical evaluation for drug-resistant temporal lobe epilepsy in our center since 2005. The patient was included only if (1) there was anamnesis of sudden, unexpected falls, (2) patient underwent long-term ECG monitoring, which did not reveal cardiac arrhythmia, (3) patient underwent surgery and was categorized as completely seizure-free after surgery, (4) the falls disappeared after surgery completely.

The interictal and ictal ECGs of these patients were compared to ECG of control group. There were age- and gender-matched patients in control who underwent surgery for drug-resistant epilepsy and were seizure-free since surgery.

Results: We identified 15 patients (7 females, 8 males) treated with temporal lobe epilepsy who reported sudden unexplained falls which completely disappeared after surgery. When analyzing ictal EEG, we identified higher tendency to ictal tachycardia in comparison to control group. No patient had ictal asystolia. No statistical significant differences were found when analyzing interictal EEG.

Conclusion: It seems that sudden unexplained falls could be rarely associated with temporal lobe epilepsy.

Disclosure: Nothing to disclose

EP2083

Cancelled

EP2084

Knowledge, attitude and practice of primary school teachers towards epilepsy in Omdurman, Khartoum state 2016

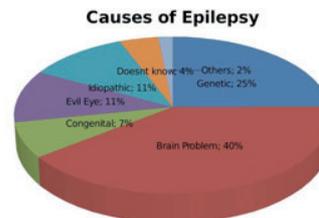
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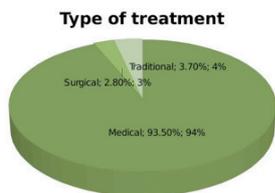
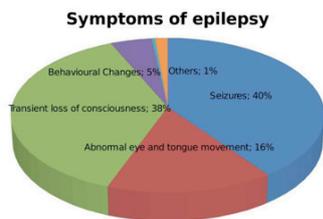
Background and aims: Epilepsy has become a rising problem and usually the first signs of epilepsy are shown in school, and hence teachers are usually the first to notice it. Objectives of this study was to assess the knowledge attitude and practice of primary school teachers on Epilepsy in Omdurman, Khartoum

Methods: This is a cross-sectional descriptive institutional study. Over a period of a week 152 questionnaires were distributed among 15 schools in the area of Abu Siid and South Omdurman, with 10 questionnaires in each school

Results: All the teachers who took part in this interview had heard of epilepsy before. The overall knowledge evaluation of teachers concerning epilepsy was reasonable with 47% having good knowledge, 50% having satisfactory knowledge, and only 3% having poor knowledge. Sadly only 15% had taken a training course on how epileptic kids should be managed. Thankfully around 75% acknowledged that epilepsy wasn't contagious and 70% would allow their kids to play with epileptic kids, reflecting positive attitude towards epilepsy. Around 40% had good management skills

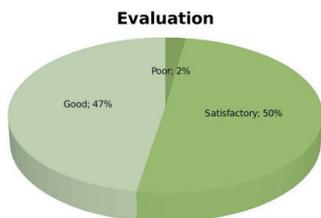


Results of causes of epilepsy by the teachers



1)Symptoms of epilepsy 2)Type of treatment

Conclusion: While many teachers had positive views about epilepsy, some negative views still persist. Furthermore, most teachers received no formal training on epilepsy. Given the potential impact that teachers’ practice and knowledge can have on children with epilepsy, further research in this area is needed. Overall, there was a generally positive attitude towards epilepsy and good knowledge on epilepsy but there were also significant deficiencies in terms of epilepsy management



Overall Knowledge Evaluation

Disclosure: University of Khartoum, Faculty of Medicine, Community Medicine department

EP2085

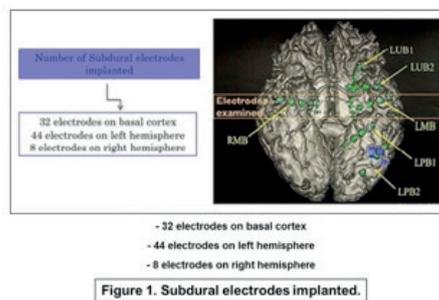
A retrieval-related evoked potential in the parahippocampal gyrus by a short-term memory task

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Background and aims: Working memory (WM) is conceived as short-term memory (STM) applied to cognitive tasks, as a multi-component system that holds and manipulates information, and as the use of attention to manage STM. Different models of WM suggest a mechanism by which a persistent spiking at cellular level could be used to hold various items. Some of these models focus on WM in the medial temporal lobe (MTL). Our purpose is to present the case of a retrieval-related evoked potential (RREP) in the parahippocampal gyrus after Gamma Knife (GK) radiosurgery and its implication on WM.

Methods: We performed this study in a patient with seizure since 2 y.o. In 2006 she was received GK for left temporal lobe epilepsy (TLE), it was not favorable. 3 years later we performed intracranial electroencephalography (iEEG) and surgery (left transsylvian selective amygdalohippocampectomy). Wada test showed right dominance (memory function). We used trapezoid electrode-sheets (“T” shape), inserted on the parahippocampal gyri (Fig 1). The patient performed two tasks whereas we recorded electrocorticogram (ECoG), picture naming task and memory task. We confirmed diagnosis of MTLE by video EEG, ECoG, MRI, CT scan, PET and SPECT.



Subdural electrodes implanted

Results: There was a large negative deflection ranging from 400 to 700ms (Figure 2). The peak latency was around 600ms. Currently 6 years later she is seizure free (Engel I).

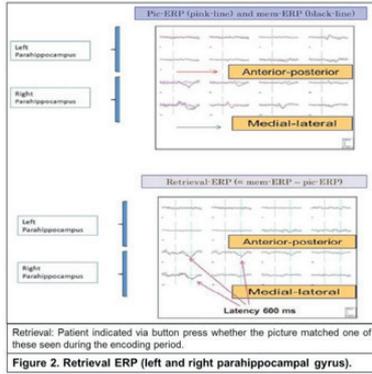


Figure 2. Retrieval ERP (left and right parahippocampal gyrus)

Conclusion: We have seen the activation (ERP) of the right parahippocampus and the absence of activity in the left parahippocampus gyrus (Figure 3); this lateralization is strongly suggested by the effect of Gamma Knife radiosurgery.

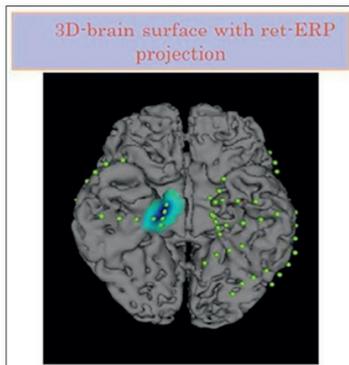


Figure 3. Activation (ERP) of the right parahippocampus

Activation (ERP) of the right parahippocampus

Disclosure: Nothing to disclose

EP2086

Sleep disorders: Clinical features and impact in epileptic patients

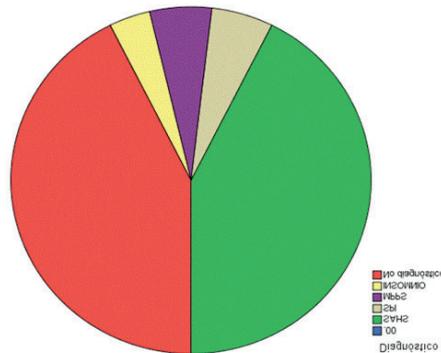
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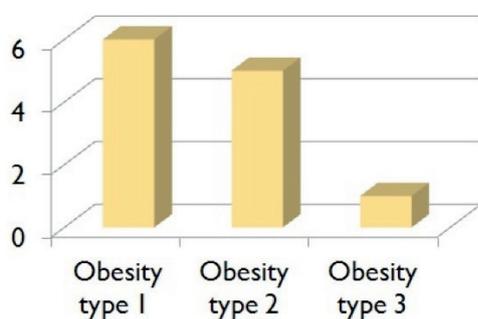
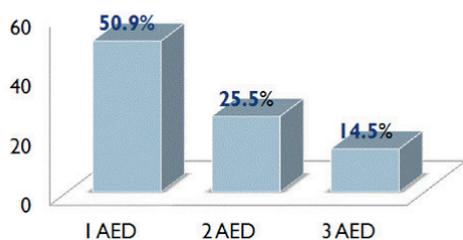
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Background and aims: Epileptic patients usually suffer sleep disorders (SD), that can affect negatively in seizure control and quality of life. Our aim is to analyze clinical features, antiepileptic therapy, symptoms, polysomnographic findings and sleep disorder in patients with epilepsy (those who were under suspicion of SD).

Methods: Retrospective descriptive observational study. We included patients that underwent monitoring in the Refractory Epilepsy Unit from January 2014 to April 30th 2016 under clinical suspicion of sleep disorder. We analyze: personal medical background, epileptic syndrome, anti-epileptic drug (AED) used, SD type, video-polysomnogram results, need of treatment and response to it, reduction of number of seizures after SD treatment.

Results: 57 patients: 30 women (54.5%). Medium age: 53 years (22-77). Non-smokers 59.3%. Obesity 21.8% (type 1 obesity 10.9%). Temporal lobe epilepsy in 45.5% (25 patients). 41.8% non-structural epilepsy. 50.9% treated with 1 AED. 46.3% seizure-free in the last year (prior to SD diagnosis). SD diagnosis: 54.38% (31). SAS (Sleep Apnea Syndrome) 45.6% (26): 42.1% OSA (Obstructive Sleep apnea). AHI (apnea-hypopnea index) 14.1 (2.7-51.8). Motor SD 15.8% (9): RLS (Restless Legs Syndrome) 33.3%, PLMD (Periodic Limb Movement Disorder) 66.6%. After treatment of SD: seizures-free 8.7% (5). Reduction >50% 7% (4)





Conclusion: Sleep disorders are a very frequent comorbidity in epileptic patients and cause an inappropriate control of seizures. Diagnosis of SD and proper treatment can affect favorably in seizures control and improve quality of life.

Disclosure: Nothing to disclose

EP2087

Cancelled

EP2088

Concept of epilepsy in Cameroonian health providers: Should we start by education?

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Background and aims: Epilepsy is a stigmatized condition Worldwide, particularly in developing countries. We aim to evaluate the general knowledge about the disease and how to manage epileptic patients in care providers of Cameroon, identifying which topics should be reinforced in their education.

Methods: We conducted an anonymous survey with demographical, social and clinical questions about epilepsy and its management to all the care providers of three Cameroonian hospitals.

Results: 38 care providers participated in the survey, 42.1% of who were female. Mean age was 40.1 y (rank 22-62). Among the causes of epilepsy, 68.4% thought that it is a psychiatric condition, 34.2% a degenerative disease, 28,9% an hereditary condition and a 21.1% secondary to an infection. About how to diagnose a patient, just a 23.7% considered that the anamnesis could be enough to set the diagnosis, being more likely in those who attended more patients ($p=0.05$). Only 60.5% considered history important for the diagnosis and a 52.6% considered necessary a positive EEG. 28,9% considered important the laboratory exams. Only a 36,8% recommended adding folic acid to pregnant woman and only 39.5% considered possible breast-feeding. The mean number of drugs known were of 2.08, being phenobarbital the most recognized.

Conclusion: The main areas that needed to be addressed in the education of care providers are the origin of epilepsy and its causes, how to diagnose a patient and how to proceed during pregnancy and patient education.

Disclosure: Nothing to disclose

EP2089

The challenge of managing epilepsy in a developing country

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Background and aims: Epilepsy is one of the most frequent conditions in developing countries. The higher frequency is associated with infections, perinatal complications and traumatic brain injury. Its management is harder because of the difficult access to complementary exams and the low availability of drugs.

Methods: Two neurologists evaluated 150 patients complaining about possible seizures in five different hospitals of the West region of Cameroon among 6 days in December 2016. We registered epidemiological and clinical data.

Results: We included 93 patients, 52.7% of whom were female. Mean age was 23.6 years (range 0-78). The relevant prior medical history was: cognitive delay 18.5%, prior CNS infections 15.2%; febrile seizures: 8.6%; perinatal complications 7.6%. Mean age of onset of seizures was 11.9 years old. Frequency of seizures was daily 5.1%, weekly 14.1%, monthly 31.1% and free of seizures 26.9%. The type episodes suggested a focal onset in 35.6%. We performed EEG to 21.5% with positive findings in 41.7%, which change treatment in 47.8% of cases. Initial treatment was phenobarbital 53.8%, carbamazepine 38.9%, phenytoin 6.4% and valproate 3.8%. We started a treatment in 15.8%, increased in 29.0%; changed in 13.2%, decreased in 5.3% and stopped in 3.9%.

Conclusion: We succeeded in making a diagnosis in a high percentage of the patients despite the lack of resources. The management is complicated and the very few diagnostic and therapeutic resources represent a challenge to the clinician.

Disclosure: Nothing to disclose

EP2090

Cancelled

EP2091

Visual illustration supporting patient-physician communication in epilepsy: A validation and reliability study of 24 seizure images, first analysis

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Background and aims: The semiological description of seizures is complicated to comprehend in words. To improve the communication between epilepsy patients and providers, 24 seizure images were developed by experts. This tool can be used during obtaining the patient's history. The objective of this study was to validate 24 seizure images before implementing into practice.

Methods: We included patients with epilepsy, persons who witnessed seizure episodes such as family members of epilepsy patients, care givers, and participants without pre-existing knowledge of epilepsy. Participants completed the questionnaire evaluating 24 seizure images twice within 36 hours. The participants were explained to choose one of the 2 items that best described each seizure image. The validity was assessed using one proportion z-test. Test-retest reliability was assessed by interclass correlation coefficient (ICC).

Results: For the initial analysis, 32 participants were included in the study. Beside two images, the proportion of correctly recognized seizure images was significantly higher than 0.7. The proportions of the two seizure images (image 9: dystonia and image 17: myoclonus) were 0.78 (95%CI 0.63-1.00) and 0.56 (95%CI 0.40-1.00). ICCs for seizure images are also high (range from 0.86 to 1.00) except for the images 9 and 17.

Conclusion: The seizure images were proved to be valid and have a high test-retest reliability. However, two images (images 9 and 17) should be revised in order to improve the validity of this tool.

Disclosure: Nothing to disclose

EP2092

The etiology of symptomatic partial epilepsy in childhood and adolescence in the Siberian region

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Background and aims: Epilepsy is polyetiological disease. The significance of various etiological factors varies in different age periods. The most important etiological factors of symptomatic partial epilepsy are brain dysgenesis, mesial temporal sclerosis, brain tumors, vascular malformations, neurocutaneous syndromes (Tuberous sclerosis, angiomas, entsefalotrigeminalny), trauma, Rasmussen's Syndrome.

Objective: To study the etiology of symptomatic partial epilepsy in childhood and adolescence in the Siberian region.

Methods: The study and dynamic observation involved 882 patients (463 boys and 419 girls) with epilepsy and epileptic syndromes. The form of epilepsy and epileptic syndromes and the etiology of symptomatic epilepsy refined during neuroimaging (magnetic resonance tomography of the brain) and functional methods of investigation (EEG with standard functional tests, video monitoring).

Results: Among the etiological factors of symptomatic partial epilepsy was a statistically significant superiority ($p < 0.05$), perinatal hypoxic-ischemic lesions (26.4%); second place is occupied by congenital abnormalities of brain development (15.9%); 8.96% were head injuries, almost the same (8.46%) - perinatal traumatic injury - Intracranial hemorrhage. Prenatal and other infectious brain damage amounted to 6.22%; hydrocephalus occurred in 3.73%; vascular pathology - 2.24% of cases. Less incidence of brain tumors (1.49%), chromosomal abnormalities (1%), hereditary neurocutaneous syndromes (0.75%) and congenital errors of metabolism (0.5%). In 14.2% of cases, the etiology of symptomatic partial epilepsy are not verified.

Conclusion: Among the etiological factors of symptomatic partial epilepsy in the Siberian region in childhood dominated by perinatal hypoxic-ischemic injury in adolescence - head injuries, mesial temporal sclerosis, and infections of the central nervous system.

Disclosure: Nothing to disclose

EP2093

The predictive value of quantitative electroencephalography (QEEG) for late-onset seizures in cobalamin mildly deficient elderly patients

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Background and aims: Cobalamin's (B12) importance for maintaining healthy nerve cells is well known. Though wide-ranging references study neuro-psychiatric complications caused by B12 deficiency, only a very few focus on EEG abnormalities and their involvement in late-onset seizures.

Purpose: Brain rhythm analysis of B12 mildly deficient elderly patients and correlation with seizures.

Methods: We evaluated the QEEG of 186 patients (mean age 73 years) with B12 gray zone levels 200-400pg/ml for the last two years. A matching healthy control sample was included. All the patients were submitted to brain imaging and EEG follow-up every 3 months.

Results: QEEG parameters of 72 (38.7%) patients were characterized by pronounced theta rhythms in the fronto-temporal regions and alpha3/alpha2 frequency ratio reduction. An increased of paroxysmal activity was observed in 26 patients and 4 of them presented seizures. After B12 supplementation EEG abnormalities subsided.

Conclusion: Mildly B12 deficiency in elderly patients causes EEG rhythm alterations. Late onset seizures occur in 5.5% of them. Considering that treatment necessity of mildly deficiency is usually underestimated, QEEG analysis is a reliable method for epileptiform activity evaluation

Disclosure: Nothing to disclose

Headache and pain 2

EP2094

Idiopathic intraorbital neuralgia: A rare cause of facial pain

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Background and aims: Infraorbital Neuralgia (IN) is an uncommon disorder, not included in the International Classification of Headache Disorders III Edition (ICHD-III, beta version). It is defined as pain in the distribution of infraorbital nerve (ipsilateral cheek, upper teeth and upper jaw), tenderness over the infraorbital notch and relief of pain by local anesthetic blockade or ablation of the nerve. We aim to analyse clinical characteristics in a consecutive series of 4 cases.

Methods: We included patients with IN attended in a headache outpatient clinic in a tertiary hospital over a 9-year period (January 2008 to January 2017). Characteristics of one of them have already been published. We prospectively gathered demographic and clinical characteristics.

Results: We identified 4 patients (2 females, 2 males) out of 4742 (0.08%) attended during inclusion period, with diagnosis of IN. Mean age at onset was 35.7±17.4 years (16-58). All of them presented tenderness over the infraorbital notch. Possible secondary causes were appropriately ruled out. Three patients suffered a burning or dull background pain, that was rated as moderate (6.3±1.5 (5-8)) on a verbal analogical scale (VAS). In two cases, lancinating exacerbations with variable frequency and rated as severe (8-9 on VAS). Regarding temporal pattern, in two patients we observed spontaneous remissions, one of them achieved a sustained response to pregabalin, and the last case has been refractory to multiple therapies.

Conclusion: Idiopathic Infraorbital Neuralgia is a quite uncommon disorder. Temporal pattern and response to treatment are variable in our series.

Disclosure: Nothing to disclose

EP2095

Case report of a patient affected by migraine with aura

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Background and aims: Migraine is a common, multifactorial, disabling, recurrent, hereditary neurovascular headache disorder. Attack often begin with warning sign (prodromes) and aura (transient focal neurological symptoms) whose origins thought to involve the hypothalamus brainstem and cortex.

Methods: We present the clinical case of a 46-year-old man suffering from childhood by migraine with aura. He had a family history of migraine and was not affected by chronic disease. He reported too memory impairment and loss of attention at work. So we planned blood tests, EEG, MRI with contrast and angiography sequences, neuropsychological and thrombophilia screening tests. Our patient had never performed neurological finding.

Results: The thrombophilic tests showed polymorphism with mutations in heterozygous, precisely FIIG20210A, MTHFR (C677T), MTHFR(A1298C) and the haplotype e2/e3. Neuropsychological tests performed (MMSE, MOCA, Frontal Assessment Battery, ADL, IADL). They showed slight deficit of short term memory and semantic memory evocation. B-vitamin biomarkers, routine blood test, EEG, and MRI scan were normal.

Conclusion: Migraine with aura is more common in women than in men. Our case is interesting because it raises questions that are important for future research. There is a difference between men and women affected from migraine with aura for the risk of ischemic stroke? The study of thrombophilic polymorphisms is useful in patients with migraine with aura? Mild memory disorders in patients with migraine with aura are predictive of cognitive decline in elderly? In this aspect, there may be a difference between men and women?

Disclosure: Nothing to disclose

EP2096

Single Pulse Transcranial Magnetic Stimulation (sTMS) for migraine: The Plymouth experience

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Background and aims: Migraine can result in economic, social, and educational losses for sufferers, as well as long term health service costs. Randomised clinical trial evidence suggests single pulse Transcranial Magnetic Stimulation (sTMS) is an effective migraine therapy. The UK National Institute of Clinical Excellence encourages the evaluation of sTMS treatment for migraine under specialist supervision. We evaluated self directed sTMS therapy for migraine on an anonymous cohort of patients in Plymouth, UK.

Methods: An anonymous questionnaire was sent to patients in receipt of the eNeura Spring Total Migraine System (TMS). The questionnaire was administered by our pharmacist. Patients were informed about the device from the headache clinic. Patients contacted eNeura Inc. to provide therapy. The device was not prescribed and was loaned by eNeura for a three month free trial period.

Results: 20% (8/39) had a significant response to sTMS therapy over 3 months. 6/8 (75%) were able to return to everyday activities with sTMS therapy. Median length of migraine history was 6-7 years receiving a median of 6 treatments prior to sTMS. 70% (27/39) did not respond to sTMS therapy over 3 months. Side effects were reported in 15% (6/39) and were headache and neck pain, as validated in sTMS safety publication.

Conclusion: sTMS does not appear to be effective for the majority of migraine sufferers in our study (70%). However for 8/39 (20.5%) of patients, sTMS was found to be of significant benefit. Identifying factors that predict response to sTMS and a local cost benefit analysis require further work.

Disclosure: Patients received a three month free trial of the eNeura Spring Total Migraine System (TMS) from eNeura Inc.

EP2097

Pseudotumor cerebri related to Behçet's disease

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Background and aims: The association of pseudotumor cerebri (PS) and Behçet's disease (BD) is extremely rare. Herein, we present the clinical and laboratory features of five patients with BD who were diagnosed as having PS.

Methods: We retrospectively reviewed 448 patients with Neuro-BD who were managed at Istanbul Faculty of Medicine between 1985 and 2015. Patients who fulfilled the diagnostic criteria for BD and PS were identified.

Results: Five patients fulfilled both criteria. The presenting symptom was headache in four of the patients. Only one patient presented with blurred vision. Four patients had papillary edema. There were no other pathologic findings in the neurologic examination. None of the patients had any parenchymal lesions. The cerebrospinal fluid (CSF) pressure was high in all patients. CSF cell counts, protein and glucose levels were normal. Only one patient had oligoclonal bands in the CSF. After the diagnosis of PS, three patients were treated with high-dose and two patients with low-dose methylprednisolone. All of the patients were treated with azathioprine, two with acetazolamide, and one with topiramate. Starting from the 15th day of treatment, all of the patients showed clinical improvement. In the long-term follow-up, one patient had headache with recurrent oral aphthous ulcers. A relapse with parenchymal involvement was observed in one patient 16 months after PS.

Conclusion: PS should be considered in patients with BD who present with elevated intracranial pressure in addition to cerebral venous sinus thrombosis and aseptic meningitis. Physicians should keep in mind that the pattern of neurologic involvement in patients with BD may change.

Disclosure: Nothing to disclose

EP2098

Patient-completed screening tools have poor diagnostic accuracy for neuropathic orofacial pain in a hospital-based cohort.

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Background and aims: Patient-completed screening tools may aid diagnosis of orofacial pain in non-specialist centres. We aimed to evaluate the diagnostic accuracy of patient-completed screening tools in a hospital-based cohort of patients referred for orofacial pain.

Methods: Prior to first appointment at a hospital facial pain clinic, patients were prospectively assigned Oregon Health & Science University (OHSU, n=152) or painDETECT questionnaires (PD-Q, n=254). The main outcome was the diagnostic accuracy of the OHSU and PD-Q compared to clinical diagnosis made by senior staff; blinded to questionnaires and validated by an independent clinician.

Results: 88 / 139 (63%) patients were correctly diagnosed by the OHSU, and 172 / 251 (69%) were correctly identified by the PD-Q to have neuropathic pain components. The OHSU had sensitivity of 0.48 (95% CI, 0.33-0.63) and specificity of 0.86 (95% CI, 0.78-0.93) to diagnose temporomandibular joint disorder, and sensitivity of 0.84 (95% CI, 0.69-0.93) and specificity of 0.59 (95% CI, 0.48-0.69) to diagnose trigeminal neuralgia. The PD-Q had an area under the receiver operating characteristics curve of 0.65 (95% CI, 0.58-0.73). Patients with a second clinical diagnosis were more likely to be diagnosed incorrectly by the OHSU (p=0.006) and PD-Q (p=0.002).

Conclusion: The OHSU and PD-Q have poor diagnostic accuracy when applied to a hospital-based cohort of patients with orofacial pain. Such patient-completed screening tools should be revalidated in non-specialist centres, prior to research or clinical applications.

Disclosure: Nothing to disclose

EP2099

Cerebral venous sinus thrombosis complicating traumatic intracranial hypotension

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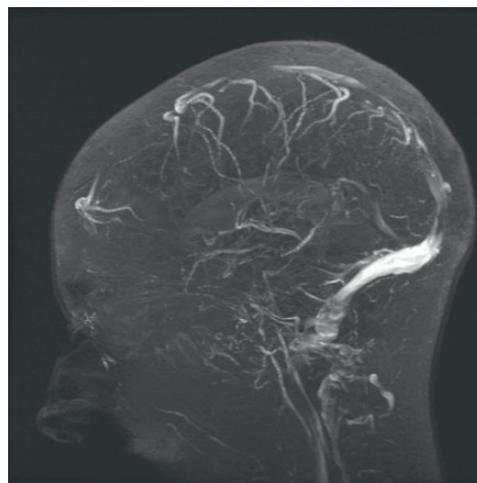
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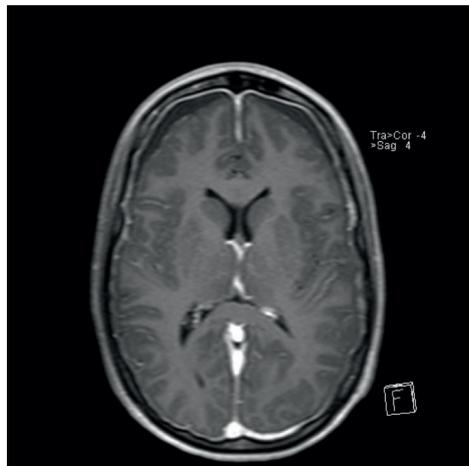
Background and aims: Cerebrospinal fluid leaks may cause intracranial hypotension and associated headache. Cerebral venous sinus thrombosis (CVST) has been described as a rare complication.

Methods: A 31-year-old woman developed severe orthostatic headache with nausea within one day after a minor head trauma. After several days, she additionally experienced headache while lying down. The patient was on an ethinylestradiol vaginal ring and was smoking for 6 months. There was a family history of venous thromboembolism.

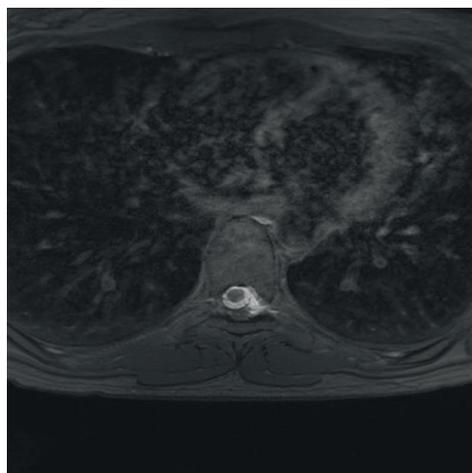
Results: Initial brain CT was normal. After the patient started experiencing headache while lying down, a cerebral MR venography demonstrated superior sagittal and left transverse sinus thrombosis (fig.1). Contrast-enhanced brain MRI also demonstrated signs of severe intracranial hypotension (fig.2). A prothrombotic disorder could not be identified. Anticoagulation with low molecular weight heparin was started and a lumbar epidural blood patch was performed. Although the headache in the recumbent position improved, the orthostatic headache remained present. A full-spine MRI with intrathecal gadolinium demonstrated an epidural CSF collection from C6 to D9 level, most prominent at level D7-D8 (fig.3). A targeted blood patch was performed at this level after which the headache subsided. MRI after 4 months demonstrated complete resolution of the CVST and signs of intracranial hypotension.



MR venography demonstrating thrombosis of the superior sagittal sinus. A coronal projection also demonstrated thrombosis of the left transverse sinus (not visible in this image).



Contrast-enhanced brain MRI demonstrating the signs of severe intracranial hypotension with meningeal enhancement and bifrontal hygroma.



Transaxial section the full-spine MR obtained after intrathecal gadolinium contrast administration. Gadolinium contrast is clearly visualized left posterolaterally to the intradural space, demonstrating a cerebrospinal fluid leak.

Conclusion: This case demonstrates the pitfalls in diagnosing intracranial hypotension with CVST. Orthostatic headache progressing into headache on lying down as well is a red flag. Imaging should be performed urgently to rule out subdural haematoma and cranial venous thrombosis.

Disclosure: Nothing to disclose

EP2100

The knowledge of residents in neurology about management of headache

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Background and aims: Headache is so common in the general population that most physicians should have a good knowledge about the management. While most patients are self-managed or managed in primary care, the most complicated patients are often referred to neurological outpatient clinics. Thus, all physicians working with neurology should have a good knowledge about headache. There is limited focus on headache in the curriculum at the four medical schools in Norway. Furthermore, approximately 50% of all residents in Norway have graduated from abroad. The national five-year training program in clinical neurology has no mandatory headache management. Therefore, knowledge and expertise in headache management must be acquired during the everyday clinical neurology training. The objectives of this survey were to investigate whether residents acquire the necessary knowledge about headache, and to evaluate experience in, and attitudes towards headache management.

Methods: The study was conducted as a questionnaire survey among all residents in neurology at all the 17 neurological departments in Norway. A contact person at each department had the responsibility for distributing and collecting the forms.

Results: All the 17 neurological departments participated, and the responder rate was over 70%. Residents answered questions about knowledge, attitudes and experiences related to headache management. Barriers to adequate headache treatment were investigated. The use of treatment guidelines and the International Classification of Headache disorders were examined. Finally, a comparison of the status of various neurological diseases was done.

Conclusion: The results are currently being analysed and will be presented at the meeting.

Disclosure: Nothing to disclose

EP2101

Cancelled

EP2102

Quality of life after withdrawal treatment in medication overuse headache: A pilot study

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Background and aims: Medication overuse headache (MOH) affects 1-2% of the population, and 30% of the patients in tertiary headache centers. It most commonly affects people with a previous primary headache disorder, most commonly migraine or tension type headache. Medication overuse results in the chronification of the primary headache, causing further disability and decreased quality of life. MOH represents a therapeutic challenge and even after successful treatment recurrence rates can be as high as 40%.

Methods: A comprehensive treatment program, consisting of acute medication withdrawal, preventive pharmacological treatment and lifestyle intervention was applied to 18 patients (15 women; mean age 40.8±14.2 years) suffering from MOH. The clinical characteristics of the headaches were recorded. Headache-related quality of life was measured using the Comprehensive Headache-related Quality of life Questionnaire (CHQQ) before and after the treatment program.

Results: After the treatment a significant reduction of the number of headache days, headache severity and analgesic consumption was observed. The CHQQ score of MOH patients, which was somewhat lower at baseline than in episodic migraine, also showed a significant increase.

Conclusion: We found significant improvement of the headache characteristics and quality of life of MOH patients completing the treatment program. Further investigations are necessary to evaluate the long-term efficacy on a bigger sample size to evaluate, if in-, or outpatient withdrawal is more effective, and follow the patients for a longer period to examine, if the results remain stable over time.

Disclosure: Nothing to disclose

EP2103

Cancelled

EP2104

Orthostatic headache? Think about intracranial hypotension

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Background and aims: Headache is a frequent clinical entity in neurology attesting to various pathologies. Its postural character is almost pathognomonic of intracranial hypotension (ICH), a rare cause of chronic headaches often misdiagnosed. Thinking about it is necessary in order to avoid severe outcomes. The aim of this case illustration is to emphasize the severity of this pathology due to her multiple complications.

Methods: We report a case of a patient with ICH diagnosed twelve years after the beginning of his symptoms, after developing several complications of his disease.

Results: This MJ patient was 51 years old. He suffers from nasal polyposis operated with ethmoidectomy. One year after his operation, he started complaining about orthostatic headache and developed epileptic seizures leading to status epilepticus twice. His MRI shows diffuse pachymeningitis with negative etiological investigations. MJ had an intractable epilepsy despite antiepileptic drugs. He was operated five years later of chronic subdural frontal hematoma without traumatic context. Finally, MJ had recently a third status epilepticus due to a cerebral venous sinus thrombosis. The diagnosis of ICH with all his complications was then retained. In front of this case and knowing the clinical history of endonasal surgery of our patient, we realized a CT of facial bones was performed. It showed an old ethmoidal breach. A surgical treatment is planned.

Conclusion: Our case shows the importance of considering ICH as an etiology of uncommon headaches in order to avoid harmful complications. Endonasal surgery may be the alarm sign leading to thinking about it.

Disclosure: Nothing to disclose

EP2105

Therapeutic use of cannabinoids - dose finding, effects and pilot data of effects in chronic migraine and cluster headache

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Background and aims: Aim was to verify therapeutic effect of 19% THC (bedrocan) + <0.4% THC, 9% CBD (bedrolite) in both prophylaxis and acute treatment of chronic cluster headache (CH) and migraine (M).

Methods: Step 1- we performed a dose finding observations in 48 chronic M volunteers, during 4 test--retest of THC+CBD. Starting dose was 10mg/orally. Step 2- M (n=370) and CH sufferers (n=190) volunteered the prospective observation. Entry criteria were: normal examines, normal electrocardiogram. After a 10-days washout period, M sufferers were randomly assigned to a 3 months-treatment with 25mg/day amitriptyline or THC+CBD 200 mg/day in 200 ml 50% fat emulsion. CH received THC+CBD or 480mg/day verapamil. One-month follow-up was provided. Two hundred mg THC+CBD were also administered as acute treatment. Rescue treatment was 6 mg/s.c. sumatriptan.

Results: Therapeutic dose was 200mg THC+CBD inducing 55% pain decrease. Doses lower than 100mg induced 0% relief. Pilot data refer to 79 M and 48 CH. In M THC+CBD prophylaxis induced 40.4% benefit versus 40.1% amitriptyline-evoked pain relief. In CH, THC+CBD prophylaxis induced scant decrease of severity and number of attacks. Acute THC+CBD decreased attack pain -43.5% in both M and CH who had an history of M when children. Relief was 0% in CH without M history. Adverse effects were drowsiness and inattention. These effects and decrease (range -70%-100%) of stomach ache, colitis and musculo-skeletal pain strictly related to female sex, $p > 0.0001$.

Conclusion: Discussion Cannabinoids may be a prophylaxis for M and an acute treatment for CH in case M occurred during childhood.

Disclosure: Nothing to disclose

EP2106

Chronic pain in patients with Parkinson's disease (PwPD): Quality of life and neuropsychiatric disturbances

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Background and aims: Psychological factors influence clinical picture, health related life quality in PwPD. Anxiety, depression are treatable, so early diagnosis and treatment improve life quality (QoL) in PwPD [Ayla Fila, 2012]. Objective was assessing neuropsychiatric profile in PwPD with chronic pain in Siberian region.

Methods: 798 PwPD are registered in movement disorders electronic database of the Siberian region. 348 non-demented PwPD were included (mean age: 65.2±6.3 years; PD mean duration: 6.8±5.8 years; H&Y stages 1-4, women:men=167:181), divided into two groups (homogeneous by gender, stage, age): I-176 PwPD with chronic pain, II-172 without. Clinical assessments were conducted using the UPDRS, H&Y Scale, MoCA-test, Beck depression inventory II, Hospital anxiety and Depression Scale(HADS-A), Apathy Scale, PD Sleep Scale, Epworth Sleepiness Scale, Parkinson's disease Questionnaire 39(PDQ-39). Chronic pain was analyzed by structured interview questionnaire.

Results: Pain was reported by 176(50.6%) participants, with 128(72.7%) reporting moderate severity or worse. The majority of PwPD had musculoskeletal pain(129 cases or 73.2%), 2(1.1%)- radicular pain, 46(26.1%)- dystonic pain, 24(13.6%)- headache. PwPD with chronic pain had higher values anxiety vs. without pain(6(4;8) vs. 10(9;12), $p < 0.0001$), the same in depression (15(11;20) vs. 20(16;27), $p < 0.0001$). Pain intensity correlated statistically significant with anxiety($r = 0.56$, $p < 0.001$), Beck depression score($r = 0.52$, $p < 0.001$), apathy ($r = 0.51$, $p < 0.001$) and health related QoL($r = 0.49$, $p < 0.001$), but not with measures of disease severity(H&YS). Moderate correlation was between pain intensity and L-dopa equivalent daily dose($r = 0.39$, $p < 0.001$), UPDRS($r = 0.46$, $p < 0.001$), lower sleep efficiency ($r = 0.43$, $p < 0.001$).

Conclusion: Musculoskeletal pain is the most common type of pain in PwPD. Disrupted sleep continuity, mood disorders, low QoL are associated with pain in PwPD.

Disclosure: Nothing to disclose

Motor neurone diseases

EP2107

Co-occurrence of ALS and LHON: Is mitochondrial dysfunction a modifier of ALS?

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Background and aims: Mitochondrial dysfunction in the pathogenesis of neurodegenerative diseases is widely investigated and mounting evidences support its contribution in early phases of amyotrophic lateral sclerosis (ALS). Here we present the unprecedented association of ALS and Leber's hereditary optic neuropathy (LHON), a maternally inherited mitochondrial disease due to complex I dysfunction.

Methods: We describe two Caucasian women affected by a sporadic form of ALS both carrying the m.11778A>G mitochondrial DNA mutation.

Results: Case 1 was affected by LHON since 26 years of age. At 73 she developed progressively worsening hyposthenia of the right lower limb, rapidly spreading to the right arm and then to the left lower limb. Bulbar signs occurred in 10 months and the patient died 18 months after onset.

Case 2 was an asymptomatic carrier of the LHON mutation. At 71 years of age she presented a bulbar onset of disease with progressive dysphagia and dysarthria. At 72 she developed proximal paresis predominant on the left side. She died 22 months after onset. A complete clinical work-out confirmed the diagnosis of ALS. Genetic testings (FUS, SOD1, TDP43 and c9orf72) were negative. El Escorial criteria for definite ALS were fulfilled for both.

Conclusion: This is the first report on a clinical association of ALS and LHON. While this association is most probably due to a chance co-occurrence of two rare diseases, the particularly aggressive course of ALS may suggest a synergistic interaction and further support the role of mitochondrial dysfunction as key in the pathogenesis of ALS.

Disclosure: Nothing to disclose

EP2108

Psychological and neuropsychological profile of ALS patients participating in a clinical trial with foetal stem cell transplantations, Phase I

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Background and aims: Intraspinal stem cells transplantation represents a new therapeutic experimental approach for Amyotrophic Lateral Sclerosis (ALS). We present the results from the psychological and neuropsychological profile of ALS patients participating to a phase I clinical trial with human neural stem cells transplantation.

Methods: 18 ALS patients with normal cognitive and behavioural profiles were recruited (years 2012 to 2015) and evaluated at the time of recruitment and followed monthly for at least one year after treatment. Patients were tested with SEIQoL-DW, Profile of Mood State, POMS and MMPI-2 questionnaires, and for cognitive functions (Cognitive Estimation CET, Raven's coloured progressive matrices, Digit span backward and forward, Verbal fluency, Verbal Judgments and Short Story tests).

Results: No cognitive or behavioral deficit emerged during the follow-up period, and quality of life main value (SEIQoL) remained high (73%, range: 69%-77%). Patients did not develop clinical depressive or anxious symptoms during time, except one subject who manifested depression mood in the post-surgery period as a reaction to the paucity of assistance received from the family.

Conclusion: Psychological and cognitive profiles remained non-problematic through time independently of the progression and severity of the disease. The surgical procedure and the lack of clear functional benefits did not affect the patients' perceived Quality of Life which remained high. In our opinion, this result can be explained with the strict clinical follow-up and psychological support given to the patients who felt especially involved in a research project and particularly cared by the specialists involved in the project.

Disclosure: Nothing to disclose

EP2109

Neurophysiological and neuroimaging techniques to monitor the safety of intraspinal foetal stem cell transplantations in Amyotrophic Lateral Sclerosis patients, Clinical Trial Phase I

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Background and aims: Intraspinal stem cells (SCs) transplantation represents a new therapeutic experimental approach for Amyotrophic Lateral Sclerosis (ALS). Given the potential iatrogenic risk and the high costs, SC clinical trials usually recruit a small number of patients; hence, objective measures of safety and effectiveness are mandatory. We present the results obtained from our neurophysiological and neuroradiological protocol applied during a phase I clinical trial with human foetal neural SCS transplantation.

Methods: Spinal cord MRI (1.5 Tesla) with fiber tracking study, and transcranial magnetic stimulation derived from the bilateral FDI and tibialis anterior muscles were performed pre and post-surgery in 18 ALS patients recruited in a phase I clinical trial with hNSCs transplantation into the cervical and spinal cord. Central motor conduction time (CMTc), Motor Evoked Potential (MEP) amplitude and CSP duration, were calculated. In addition, we applied during the surgery a standard neurophysiological protocol including Somatosensory Evoked Potential obtained by stimulation of posterior tibialis and median nerve, and MEP with transcranial electrical stimulation.

Results: No patient manifested any clinical side effects during or after surgery. Amplitude and onset of cortical and radicular MEP such as CMTc did not change during and following surgery. MRI showed no modification of spinal cord morphology and DTI values.

Conclusion: The results obtained from neurophysiological and neuroimaging techniques are equally reliable to monitor the possible short-term side effects by surgery. Therefore, we believe future Phase II Clinical Trial could make use of neurophysiological tests only in the short-term monitoring of surgery because easier to perform, and cheaper.

Disclosure: Nothing to disclose

EP2110

The CSF values of advanced oxidation protein products and total thiol content in ALS patients

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Background and aims: Oxidative stress (OS) is considered as one of the most challenging hypothesis in pathogenesis of ALS. The aim of this study was to contribute to the understanding of what extent there is involvement of OS in ALS.

Methods: We assessed biomarkers of oxidative stress - Advanced Oxidation Protein Products (AOPP) and total thiol content (SH) in CSF of 24 ALS patients and 20 controls. Thirteen patients presented with the spinal form of the disease, while the remaining eleven patients had bulbar form.

Results: CSF AOPP levels were higher than those in control group (CG), while SH groups showed lower values compared to CG ($p < 0.001$). When different clinical presentations were compared, AOPP values were higher in patients with bulbar compared with patients with common spinal manifestation ($p < 0.001$). There were no differences in SH group's levels among different clinical forms. Significant negative AOPP and the SH group correlation was confirmed in ALS patients ($p < 0.01$), especially in bulbar group ($p < 0.01$). Significant mild correlations between tested parameters and functional rating scale and index of disease progression were recorded for both of tested parameters in spinal form of ALS ($p < 0.01$), and were more pronounced for the levels of SH groups.

Conclusion: The data support that OS is involved in the pathophysiology of ALS. CSF AOPP level may serve as useful biomarker of damage to the brain stem motor neurons. Neither AOPP nor SH groups in CSF of ALS patients can be used as certain biomarkers to assess disease progression.

Disclosure: Nothing to disclose

EP2111

Early-onset Hirayama disease in a female

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Background and aims: Hirayama disease (HD) is a rare myelopathy, occurring predominantly in males with onset in the teens.

Methods: Case report

Results: Here we present a 17yo Caucasian female patient who developed the first signs of HD at 10.5y of age. Prior to onset she had experienced a growth spurt and grew about 8 cm. At the age of 12y more obvious weakness of the hands, predominately on the left side, developed. Weakness increased in cold weather and the hands were often cold and sweaty. No sensory deficit was noticed. Neurological examination at age 13y revealed marked weakness (MRC 2 to 3-) for extension of the index and middle fingers bilaterally and for abduction of the left thumb. Additionally, there was weakness (MRC 3+ to 4) for extension of the ring and little fingers bilaterally, for abduction of the right thumb, and for abduction and adduction of the left fingers II-V, and flexion of the left fingers II-V. Postural tremor and poly-mini-myoclonus of the fingers on extension could be seen. There was marked wasting of the right thenar and mild wasting of other intrinsic hand muscles. The disease further progressed over the next years and the typical clinical, electrophysiological and neuroimaging signs of HD were found. After this period - and achievement of her final height, no further progression was noticed.

Conclusion: Pediatric neurologists should be aware of HD, which can also occur in girls in early adolescence. Prognosis of HD in females is fair and not at variance from males.

Disclosure: Nothing to disclose

EP2112

Mitochondrial disorder may mimic amyotrophic lateral sclerosis at onset

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Background and aims: Mimicry between mitochondrial disorder (MID) and amyotrophic lateral sclerosis (ALS) fades away with disease progression and development of mitochondrial multi-organ-disorder-syndrome. If the arising multio-organ involvement is mild, MID still may be misinterpreted as ALS.

Methods: Case report

Results: A 48 years old male developed slowly-progressive weakness, wasting and fasciculations initially on the left upper limb, which spreaded to the shoulder-girdle and the lower limbs. Since he additionally developed tetraspasticity, bulbar involvement, and electrophysiological investigations were indicative of a chronic neurogenic lesion, he was diagnosed as ALS. Re-evaluation by muscle biopsy because of features incompatible with ALS, such as hyperhidrosis, thyroid dysfunction, hyperlipidemia, and sensory involvement, revealed morphological features indicative of a MID and a combined complex-II/III defect. A MID was suspected since combined complex-II/III defect has not been reported in patients with ALS.

Conclusion: MID may mimic ALS at onset of the disease and may start as a mono-organ disorder to turn into a multi-organ disease after long-term progression. A combined complex-II/III defect may manifest with bulbar involvement.

Disclosure: Nothing to disclose

EP2113

Rehabilitation in ALS patients: Effects on circulating microRNAs

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Background and aims: Amyotrophic lateral sclerosis (ALS) is a rare, progressive, neurodegenerative disorder caused by degeneration of upper and lower motoneurons. The effects of exercise and rehabilitation in patients with ALS are still debated. A moderate and regular exercise is supported in the treatment of many neuromuscular diseases. We previously conducted microRNAs studies in ALS patients and we observed differences in myomiRNAs levels in spinal versus bulbar onset. In this study we analysed the role of circulating myomiRNAs after physical rehabilitation

Methods: We measured muscle specific microRNAs (miR-1, miR-206, miR-133a, miR-133b) by Real Time PCR in 19 ALS patients (12 male, 7 female). We analysed the levels of these microRNAs in serum collected before (T0) and after (T1) a period of 6-8 weeks of rehabilitation

Results: We observed a general down-regulation of all miRNAs studied after rehabilitation. In our population myomiRNAs decreased in a similar manner in male and female patients, therefore no gender effect was found. On the contrary the age of patients under study was found to be relevant: patients under 55 years old have a more marked decrease in myomiRNAs levels than patients with older age.

Conclusion: We have found that microRNAs are an important tool to monitor rehabilitation in ALS patients and suggests a positive effect of the treatment. There seems to be a more pronounced decrease in myomiRNA levels in patients with younger age in this motoneuron disease after physical rehabilitation. Further study are needed to correlate circulating microRNAs with muscle atrophy and to confirm age differences.

Disclosure: Nothing to disclose

EP2114

Granulocyte colony-stimulating factor for Amyotrophic Lateral Sclerosis: A randomized, double-blind, placebo-controlled study of Iranian patients

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Background and aims: The aim of this study was to determine the efficacy and tolerability of granulocyte colony-stimulating factor (G-CSF) in subjects with amyotrophic lateral sclerosis (ALS)

Methods: Forty subjects with ALS were randomly assigned to two groups, which received either subcutaneous G-CSF (5 µg/kg/q12h) or placebo for 5 days. The subjects were then followed up for 3 months using the ALS Functional Rating Scale-Revised (ALSFRS-R), manual muscle testing, ALS Assessment Questionnaire-40, and nerve conduction studies. CD34+/CD133+ cell count and monocyte chemoattractant protein-1 (MCP-1) levels were evaluated at baseline.

Results: The rate of disease progression did not differ significantly between the two groups. The reduction in ALSFRS-R scores was greater in female subjects in the G-CSF group than in their counterparts in the placebo group. There was a trend toward a positive correlation between baseline CSF MCP-1 levels and the change in ALSFRS-R scores in both groups (Spearman's $\rho=0.370$, $p=0.070$).

Conclusion: With the protocol implemented in this study, G-CSF is not a promising option for the treatment of ALS. Furthermore, it may accelerate disease progression in females.

Disclosure: Nothing to disclose

EP2115

Cancelled

EP2116

Brain white matter demyelinating lesions and amyotrophic lateral sclerosis in a patient with C9orf72 hexanucleotide repeat expansionM. Oliveira Santos¹, I. Caldeira², M. de Carvalho¹

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Background and aims: A hexanucleotide repeat expansion in the C9orf72 gene has been associated to amyotrophic lateral sclerosis (ALS) and frontotemporal dementia. The association of multiple sclerosis (MS) and ALS with C9orf72 expansion was described before in four subjects. However, C9orf72 is not associated with increased risk of MS. Inflammatory pathways related to NF- κ B have been linked to ALS and MS, and appear to be important in C9orf72-ALS patients.

Methods: Case Report

Results: A 42-year-old woman presented with progressive bulbar symptoms for 9 months. Past familial and personal medical history were unremarkable. Neurological examination disclosed severe spastic dysarthria, atrophic tongue with fasciculations, brisk jaw and limb tendon reflexes, and bilateral Hoffman sign. Brain MRI revealed bilateral, multiple periventricular and juxtacortical changes, configuring a MS-like pattern. Some of them showed gadolinium enhancement. Needle EMG sampling confirmed chronic neurogenic changes involving cranial-innervated muscles. Blood tests were unremarkable. CSF was normal, with no oligoclonal bands. Visual and somatosensory evoked potentials disclosed no abnormalities. Six months later, brain MRI was performed and no new demyelinating or gadolinium-enhancing lesions were identified. Genetic screening revealed a C9orf72 expansion.

Conclusion: This sporadic bulbar-onset ALS, with C9orf72 expansion, revealed white matter abnormalities on brain MRI suggestive of MS. As no clinical manifestation of MS was identified, a diagnosis of radiologically isolated syndrome would be considered. We speculate that these demyelinating lesions might facilitate expressivity of C9orf72 expansion, through NF- κ B activation. This plausible association may lead to the identification of a therapeutic target in this subgroup of C9orf72-ALS patients.

Disclosure: Nothing to disclose

EP2117

Amyotrophic lateral sclerosis (ALS) in patient with dermatomyositisC. Papastergios, B. Chlopicki, M. Bergelin-Axelsson
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Background and aims: ALS causes the fast degeneration of both upper and lower motor neuron. Many mechanisms have hypothesized to participate in pathogenesis while concurrent presence of ALS and other diseases including multiple sclerosis, frontotemporal dementia and myasthenia gravis has been described.

Methods: We present a case of ALS in a patient who had already dermatomyositis diagnosis.

Results: A 69 years old man was admitted to our department with a five-month history of dysarthria and swallowing difficulty. The patient had a dermatomyositis diagnosis established fifteen years ago, based on both clinical features and biopsy. He was treated with MTX and methylprednisolone initially. The last two years MTX dose was 5mg weekly as patient was asymptomatic. After clinical deterioration MTX dose increased to 25mg weekly. On first assessment to our department he presented right foot drop, fasciculations in arms and legs, bilateral Hoffman sign and hyperreflexia. MRI brain showed no signs of intracranial pathology. Blood tests were normal, while lumbar puncture revealed increased neurofilament. Electrophysiological studies showed presence of fibrillations, positive sharp waves and fasciculations. New clinical control further revealed muscle weakness, unilateral positive Babinski sign and tongue fibrillations. Biopsy didn't show any signs of active inflammatory myopathy. Eventually ALS diagnosis was set and the patient started treatment with riluzole.

Conclusion: To our knowledge this is the first time that dermatomyositis and ALS are present to the same patient. Further studies are required to establish a potential connection between inflammatory myopathies and ALS.

Disclosure: Nothing to disclose

EP2118

Five cases of motor neuron disease associated with a neoplastic process

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Background and aims: Motor Neuron Disease (MND) and neoplastic processes association is rarely described.

Methods: We retrospectively analyzed 35 patients with MND followed in our Hospital since 2013.

Results: A neoplastic process was found in five patients.

Case1: 54 years old (y/o) female, had breast tumorectomy and radiotherapy in 2005 due to invasive ductal breast cancer (IDBC), BRCA2 mutation-related. The IDBC relapsed in 2015 implying bilateral mastectomy. After one month, develops symptoms of upper and lower (U+L) MND affecting bulbar, cervical, dorsal and lumbosacral (B+C+D+LS) segments. Onconeural antibodies were weakly positive for anti-PNMA2. Case2: 52 y/o female with U+L MND signs in C+D+LS segments in 2013. A thymoma was diagnosed in December 2016. Onconeural antibodies and anti-VGKC (anti-CASPR2 and anti-LG11) were negative. Case3: 47 y/o male developing lower MND signs affecting B+C+D+LS segments starting in 2015. Onconeural antibodies were positive for Anti-Yo. A Hürthle cell follicular thyroid carcinoma was diagnosed in 2016 being submitted to hemithyroidectomy followed by two cycles of IVIg. Case4: 74 y/o female diagnosed with IDBC in 2014, submitted to mastectomy, radiotherapy and hormonotherapy. In 2016 initiates rapidly progressive symptoms of U+L MND affecting B+C+D+LS segments. Onconeural antibodies not performed. Case5: 71 y/o male presented with U+L MND affecting B+C+D+LS, in 2010. Diagnosed with lung adenocarcinoma in 2011 and submitted to chemo and radiotherapy. He died in 2016. Onconeural antibodies not performed.

Conclusion: In our cohort, 14.3% of MND patients were diagnosed with a neoplastic process. Treating the neoplastic process may potentially halt or reverse the progression of MND.

Disclosure: Nothing to disclose

EP2119

Possible contribution of NO system in the pathogenesis of spinal muscular atrophy, type 2, in in vitro experiments

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Background and aims: Investigate the effect of the substance - RSPU-260 - that increases the activity of endothelial NO-synthase in the condition of organotypic cultivation of spinal ganglia in the medium containing plasma of the patients SMA type 2.

Methods: Objects of the study were the plasma of 12 patients of SMA type 2 and 1200 sensory ganglions of 10-12-day chicken embryos cultivated for 3 days. Control explants were cultivated in a nutrient medium of standard composition. We have added blood serum of 2 type SMA patients to cultural medium in 600 test dishes. The agent RGPU-260 in concentration 10⁻⁷ or 10⁻⁵ M was added to the culture medium on the plates together with blood serum in a part of experiments. The data were processed with STATISTICA 68.0 and Student's t-test at p=0.05.

Results: The blood serum of 12 patients with SMA, type 2, at dilutions of 1:2, 1:10, 1:50 completely blocked the growth of neurites of sensory ganglia. With further dilution of 1:100, the blood serum did not affect the growth of neurites. The cultivation of explants of spinal ganglia in the growth medium containing the blood serum at a dilution of 1:70 and RSPU-260 (10⁻⁵ M), revealed positive elimination of inhibition of neurites by the serum.

Conclusion: There was no inhibition of neurites by the blood serum with RSPU-260, which increases the activity of endothelial NO-synthase, in concentration (10⁻⁵M). Thus, the model conditions revealed neuroprotective effects of NO system, apparently mediated by the change of activity of endothelial NO-synthase.

Disclosure: Nothing to disclose

EP2120

Hirayama disease as an ALS-like syndrome

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Background and aims: Hirayama disease (HD) is a slowly progressive benign motor neuron disease that affects the distal upper limb. The gradual onset, progressive course of the disease, and isolated motor neuron involvement may mimic early stage of the amyotrophic lateral sclerosis (ALS).

Methods: Clinical case

Results: A 25-year-old woman presented with evident weakness and hypotrophy in her left arm (more pronounced in the hand) with muscle cramps caused by cold temperature, which slowly progressed for 8 years (Fig. 1). Nerve conduction study revealed signs of damage of the left ulnar nerve with velocity reduction at the elbow joint. Needle electromyography revealed signs of moderate active denervation and fasciculation potentials only in the muscles innervated by the ulnar nerve. Signs of reinnervation were also found at the cervical segments, which are typical for anterior horn disfunction. MRI of the cervical spine was unremarkable. ALS was diagnosed. Later MRI revealed spinal cord flattening and T2-hyperintensity at the C5-C6 levels in neutral position (cervical lordosis was normal and epidural space was not enlarged); in flexion position, displacement of the posterior dura was visualized (Fig. 2). T2-hyperintensity focus was revealed intramedullary at the same level in the left anterior horn (Fig. 3). Thus HD was diagnosed.



Fig. 1. Hypotrophy of left hand



Fig. 2. MRI of the cervical spine in neutral and flexion position

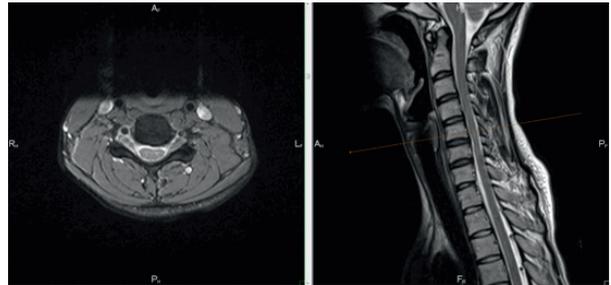


Fig. 3. MRI - T2-hyperintensity myelopathy focus

Conclusion: HD is a rare condition with clinical presentation similar to ALS, however it has specific signs described by K. Hirayama. The neurologists and MRI-specialists should be more informed about HD given the importance of its early diagnosis.

Disclosure: Nothing to disclose

Movement disorders 3

EP2121

Speech and voice response to levodopa in late-stage Parkinson's disease patients: Report from an acute levodopa challenge

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Background and aims: Parkinson's disease (PD) patients are affected by hypophonia, dysprosody and dysarthria that worsen with disease progression. The influence of levodopa on the quality of speech is inconclusive, and no data are available for late-stage PD (LSPD).

Methods: LSPD patients (Schwab and England ADL Scale (SE) ≤ 50 or Hoehn Yahr (HY) Stage >3 (MED ON)), underwent a levodopa challenge with a supra-maximal dose (150%). Before and after levodopa intake, each participant performed several vocal tasks selected from the European Portuguese version of the Frenchay Dysarthria Assessment version 2 in order to assess: respiratory support for speech, voice quality, voice stability, voice variability and speech rate. Motor performance was evaluated by the MDS-UPDRS part III. All voice samples were recorded using a tabletop unidirectional microphone and analyzed by a speech and language therapist blinded to patients' therapeutic condition using the Praat 5.1 software.

Results: Twenty-four of the twenty-seven LSPD patients included in the study succeeded in performing the voice tasks. Clinical characteristics are detailed in Table I. A positive correlation was found between disease duration and voice quality ($R=0.8$; $p<0.05$) and variability ($R=0.793$; $p<0.05$). Levodopa significantly improved the MDS-UPDRS-III score (20%), with a beneficial effect on axial signs with the exception of speech, but no improvement was found by means of automated analysis (Table II).

Patients data	LSPD (n=24)	LSPD MALE (n=14)	LSPD FEMALE (n=10)	p-value
Age (yrs)	79 [71.5-81.7]	77.5 [70.7-81.2]	79 [73.5-85]	ns
Age at disease onset (yrs)	64.5 [54.5-69.5]	62.5 [55-67]	65 [51.5-71.5]	ns
Disease duration	14.5 [11-15.7]	13.5 [8.7-17]	15 [11.7-17.2]	ns
Education (yrs)	4 [4-11]	4 [4-12]	5 [4-10.5]	ns
S&E (ON/OFF)	40/35 [40-40.7 / 22.5-40]	40/30 [40-40 / 40-40]	40/30 [27.50 / 17.5-50]	ns
HY (ON/OFF)	4 [2-4] / 4 [2-4.75]	3 [2-4] / 3 [2-4]	4 [4-5] / 4 [4-5]	ns
PDD (n (%))	14 (58%)	10 (71%)	4 (40%)	ns
MMSE	22.5 [21.2-25]	22.5 [22.5-24]	22.5 [18.5-27]	ns
MMSE (demented/non-demented)	22 [17-23.7] / 25 [23-26.7]	22 [21.7-24.3] / 23 [22.2-25.2]	17 [13-19.3] / 27 [25-28.5]	ns
LEDD (mg)	1037 [902-1272]	1100 [990-1303]	905 [742-1257]	ns
MDS-UPDRS-II	31 [27-38]	32 [29.2 - 38.5]	30 [26.5-38]	ns
MDS-UPDRS-III (MED ON/MED OFF)	50 [40-54] / 64 [52-77]	50 [42.5-55.2] / 61 [53-76]	50 [37.5-62.5] / 64 [48-79.5]	ns
Axial sign (MED ON/MED OFF)	8 [6-13] / 10 [7-13]	8 [6-13] / 10 [7-13.2]	8 [6.5-12] / 10 [7-13.5]	ns
MDS-UPDRS-IV	4 [2-9.5]	5 [2-8.5]	4 [0-11.2]	ns

Table I. Values are presented as median [IQR, 25th-75th percentile] if no otherwise specified; ns: not significant. LEDD: L-dopa equivalent daily dose; PDD: Parkinson's disease with dementia; MMSE: mini mental state examination; S&E: Schwab and England score; HY: Hoehn Yahr Stage. P value is the results for male vs. female scores's comparison.

Table.I

	LSPD patients (n=24)		p-value
	MED OFF	MED ON	
MDS-UPDRS-III	50 [40-54]	50 [40-54]	<0.001
Speech	2 [1-3]	2 [1-3]	0.8
Prosodic quality	3 [1-6]	2 [1-3]	<0.05
Prosodic stability	3 [2-4]	3 [2-3]	<0.05
Coar	3 [2-4]	3 [2-3]	<0.05
Axial signs	10 [7-13]	8 [6-13]	<0.05
HY	4 [2-4.75]	4 [2-4]	0.7
Voice Respiratory support for speech Voice duration (sec)	5.8 [4-11.7]	7 [3.6-10.6]	0.6
Voice stability			
Pitch break time	1.2 [0.2-0.6]	0.8 [0.07-0.5]	0.9
UDFS	2.4 [1.6-6]	2.3 [1.5-5.1]	0.8
Flow	0.8 [0.5-1.2]	0.7 [0.4-1]	0.3
Voice quality F0 average	134 [120-200]	142 [147-202]	0.2
Voice variability Standard/F0/2	31 [18-51]	39 [20-60]	0.5
Speech rate	7 [3.6-5.6]	7 [4.2-7.7]	0.2

Table 2. Values are presented as median [IQR, 25th-75th percentile]. Statistical significant results are in bold. Axial Signs: sum of item 3.1, 3.10-3.12 of the MDS-UPDRS-III. P-value is the results of MED OFF versus MED ON scores.

Table.II

Conclusion: Speech is severely affected among LSPD patients. Although levodopa still had some effect on motor performance, no improvement was found on speech neither by means of a clinician rating scale nor by automated analysis.

Disclosure: Nothing to disclose

EP2122

Fatigue assessment and risk factors in Parkinson's disease

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Background and aims: Fatigue is a frequently encountered non-motor symptom in Parkinson's disease (PD). There are several scales designed to assess fatigue.

Objectives: the aim of this study is to evaluate the severity of fatigue in patients with Parkinson's disease as well as possible risk factors and the impact on quality of life.

Methods: Prospective study on 52 patients with PD. Fatigue was assessed using Fatigue Symptom Inventory (FSI).

Results: The study included 30 males (58%), with mean age of 61.7 years. For the first part of the scale (questions 1-4), most of the patients rated a moderate level of fatigue (5 out of 10 points on the rating scale). Regarding the perceived interference with quality of life, most of the patients rated a mild-to moderate impact of fatigue (mean of 3.6 out of 10 points for males). Most of the patients (36.3% males, 27.2% females) felt fatigued during three out of seven days, considering the previous week as the reference interval. The patients felt the fatigue mostly during evening. Levodopa equivalent dose and depression are independent risk factors for presence and degree of fatigue.

Conclusion: Fatigue is an important symptom reported by the patients with PD and it impairs quality of life to various degrees.

Disclosure: Nothing to disclose

EP2123

Autoimmune haemolytic anaemia related to apomorphine

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Background and aims: Case report of autoimmune haemolytic anaemia (AIHA) secondary to apomorphine. Well-Known entity related to L-dopa and rarely cause by apomorphine.

Methods: A 62-year-old patient with idiopathic Parkinson disease (IPD) of 10 years of evolution treated with L dopa/carbidopa/Entacapone (375/93,75/600mg per day) and continuous subcutaneous infusion of apomorphine began in June of 2015 (6.5 mg/h during 12 h; total daily apomorphine: 78 mg) maintaining low disability in Schwab & England Scale (90%). In November 2016 was admitted to hospital by hemodynamic angina secondary to severe anaemia (haemoglobin 6.9mg/dl). The haematological studies conclude that presents an AIHA. After ruling out autoimmune diseases, infections or neoplasms associated, the aetiology was interpreted as pharmacological, withdrawing levodopa/carbidopa/entacapone, and starting therapy with methylprednisolone, immunoglobulins, and rituximab. Three weeks later a severe anaemia persisted requiring transfusion; consequently, we finally removed apomorphine and added levodopa/carbidopa, with what the haemoglobin level improved.

Results: Haemoglobin levels after 3 months since the withdrawal of apomorphine were normal so that we attach to this drug cause AIHA. The literature reviewed, shows only 1 case secondary to apomorphine after 6 months of treatment, in our case the AIHA occurred after 17 months.

Conclusion: The apomorphine infusion is a therapy used for EPI, with favourable clinical outcome and safe use, even though there are described range of adverse effects. In spite of the rarity of this complication, it must be recognized, because of may compromise the patient's life. The apomorphine in this case should be suspended valuing other therapies for advanced IPD.

Disclosure: Nothing to disclose

EP2124

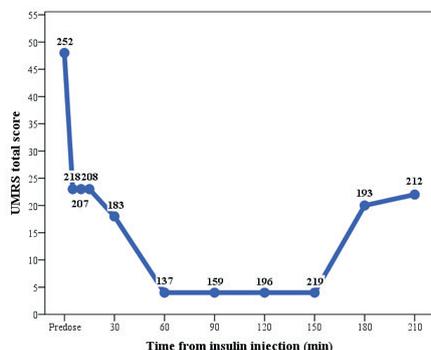
Myoclonic dystonia (DYT11) responsive to insulin therapy. A case-report

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 University of Brescia, Brescia, Italy

Background and aims: A 44-year-old male has been followed for myoclonic dystonia (DYT11) due to a heterozygous pathogenic mutation in the epsilon-sarcoglycan gene (SGCE, NM_003919.2:c.1114C>T). At the age of 44, the patient developed diabetes mellitus type 1, and therefore insulin regimen was started. At each administration of subcutaneous rapid insulin, he reported symptoms' relief, which persisted throughout the insulin effect. We wondered whether the symptom improvement were due to either the reduction of glucose levels or to an insulin-mediated effect.

Methods: After insulin injection and for the next 3.5 hours, a videotape of clinical symptoms along with capillary blood glucose determinations was carried out. Myoclonus was evaluated with the Unified Myoclonus Rating Scale (UMRS).

Results: As reported in Figure1, symptoms clearly improved few minutes after insulin injection. Symptoms remained stable for about three hours, when myoclonus progressively reappeared. We did not find any correlation between UMRS total score and capillary blood glucose levels, while the correlation with time from insulin injection resulted significant (Spearman's $\rho = -0.629$, $p = 0.038$).



Conclusion: At our best knowledge, insulin-mediated improvement of myoclonus has never been reported. Even though the brain has been considered a former non-classical insulin responsive tissue, it is now recognized as an insulin sensitive organ. In the brain, insulin might exert neuromodulating effect. Albeit these considerations are theoretical, this is the first report arguing for a possible direct insulin effect on myoclonic symptoms. This intriguing association could open new perspectives for treatment of myoclonus or, at least, for myoclonus due to SGCE mutations.

Disclosure: Nothing to disclose

EP2125

Features of speech in Wilson's and Parkinson's diseases revealed by spectral analysis

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Background and aims: Speech impairment occurs in Wilson's and Parkinson's diseases (WD and PD) and may manifest as dysphonia (due to worsening of larynx muscles control) and dysarthria (due to worse control of airways and oral cavity resonance qualities). In the «source-filter» model human speech apparatus is considered as consisting of independent sound source (larynx), linear filter (oro- and nasopharynx, nasal passages, oral cavity), and emitter (mouth). The objective of the research was to study speech impairment in PD and WD, utilizing digital spectral voice analysis.

Methods: Speech was recorded digitally with 16kHz quantization rate while counting from 1 to 30. Calculations were performed using scripts in R language. Spectral analysis was performed on 50ms samples, with step between samples being 10ms; samples which contain speech were detected automatically. For each sample we estimated voice fundamental frequency (FF) using cepstral analysis, and evaluated results for presence of irregular fast FF changes, voice interruptions, and periods of absent FF while vowel pronunciation. Using conventional spectral density estimation, we calculated frequencies F25 and F75, for which intervals [200Hz;F25] and [200Hz;F75] contain 25% and 75% of power in the range [200Hz;4000Hz] respectively.

Results: We studied 29 PD and 35 WD patients. Disturbances of voice production were found in 20 PD patients (69.0%) and 25 WD patients (71.4%). Number of F25-F75 clusters less than 5 (which reflect disturbance of articulation) was found in 8 PD patients (27.6%) and in 18 WD patients (51.4%).

Conclusion: Spectral analysis is a useful tool for speech assessment in PD and WD.

Disclosure: Part of the research on Wilson's disease was done while the visit to the Institute of Psychiatry and Neurology (Warsaw, Poland), which was funded by the EAN Clinical Fellowship program.

EP2126

The Prevalence of Restless Legs Syndrome in Edirne and its districts: concomitant comorbid conditions and secondary complications

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Background and aims: We aimed to determine the prevalence and riskfactors of restless legs syndrome in Edirne and its districts, located in Western Thrace, which is the most western part of Turkey.

Methods: In this study, 4003 individuals who could communicate and agreed to participate in the study were evaluated. To obtain the data from the applicants in 30 Family Health Centres in Edirne and its districts, a face-to-face questionnaire that consisted of 54 questions was prepared by the researchers. The questionnaire included general information, questions to evaluate potential concomitant comorbid conditions and questions regarding the symptomatology used in restless legs syndrome (RLS) diagnosis, as well as questions to evaluate insomnia and tension-type headache secondary to insomnia according to the ICD-II Criteria (International Classification of Sleep Disorders-II Criteria).

Results: Of 4003 individuals, 282 were diagnosed with RLS according to the questionnaire results from Edirne and its districts, and the prevalence of RLS was 7%. Approximately, 47.9% of the patients with RLS were male, and 52.1% were female, which was not significantly different ($p > 0.05$). Anaemia was identified in 41.1% of the cases and control group was detected in 19.4%, which was significantly different ($p < 0.001$). Secondary insomnia was identified in 64.2% of the cases with RLS and was not detected in 35.8%, which was significantly different ($p < 0.001$).

Conclusion: RLS prevalence studies will increase the awareness of the community and provide early diagnosis and treatment, as well as serve as a basis to reduce morbidity and improve the quality of life.

Disclosure: Nothing to disclose

EP2127

A case of hereditary tyrosinemia type 3 in an adult patient with atypical parkinsonism

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Background and aims: Tyrosine is an aromatic amino acid important in the synthesis of catecholamines, thyroid hormones and melanin. Hereditary tyrosinemia type 3 is a rare autosomal recessive disorder caused by deficiency of 4-hydroxyphenylpyruvate-dioxygenase (HPD), the second step in the tyrosine catabolism pathway that may result in elevated plasma tyrosine concentrations. The affected patients have neurologic dysfunction: ataxia, tremor, seizures, mild psychomotor and mental retardation. Treatment consists of a diet low in tyrosine and phenylalanine.

Methods: 54-year-old man with arterial hypertension and obstructive sleep apnea who presented from childhood cephalic, lips and limbs tremor. His parents were consanguineous. His father was diagnosed with essential tremor and his brother had mental retardation and general tremor. In the last years our patient presented hypersomnia, generalized slowness of movement, ataxia and worsening tremor. He also had decreased verbal fluency and apathy. Clinical signs and symptoms were compatible with a tremoric hypokinetic syndrome with cognitive impairment and depression.

Results: Tests showed: elevated tyrosine concentrations (plasma: 553 micromol/L, urine: 0.91 mmol/g), moderate cognitive impairment (neuropsychological-tests) and mutation in homozygosis in exon 8 of the HPD gen (c.479A>G)(p.Try160Cys). Cranial magnetic resonance imaging and DaTSCAN were normal. We started diet and symptomatic treatment.

EXCRECION DE AMINOACIDOS FISIOLÓGICOS E			
GLUTAMICO	0,02	mmol/g creatinina	(0,00-0,11)
HIDROXIPROLINA	0,02	mmol/g creatinina	(0,00-0,11)
SERINA	0,20	mmol/g creatinina	(0,00-0,42)
ASPARRAGINA	0,09	mmol/g creatinina	(0,00-0,38)
GLICINA	0,56	mmol/g creatinina	(0,00-2,40)
GLUTAMINA	0,33	mmol/g creatinina	(0,00-0,81)
TAURINA	1,05	mmol/g creatinina	(0,00-1,50)
HISTIDINA	0,62	mmol/g creatinina	(0,00-1,10)
CITRULINA	0,01	mmol/g creatinina	(0,00-0,10)
ALANINA	0,23	mmol/g creatinina	(0,00-0,51)
ARGININA	0,01	mmol/g creatinina	(0,00-0,04)
PROLINA	0,01	mmol/g creatinina	(0,00-0,12)
3-METIL-HISTIDINA	0,32	mmol/g creatinina	(0,00-0,35)
TIROSINA	0,91	*mmol/g creatinina	(0,00-0,14)
VALINA	0,04	mmol/g creatinina	(0,00-0,10)
METIONINA	0,00	mmol/g creatinina	(0,00-0,03)
CISTINA	0,03	mmol/g creatinina	(0,00-0,15)
ISOLEUCINA	0,01	mmol/g creatinina	(0,00-0,02)
LEUCINA	0,01	mmol/g creatinina	(0,00-0,06)
FENILALANINA	0,02	mmol/g creatinina	(0,00-0,16)
TRIPTOFANO	0,03	mmol/g creatinina	(0,00-0,09)
ORNITINA	0,00	mmol/g creatinina	(0,00-0,05)
LISINA	0,03	mmol/g creatinina	(0,00-0,35)

Image 2: Tyrosine concentrations urine

PERFIL DE AMINOACIDOS			
ASPARTICO	32	*umol/L	(6-22)
GLUTAMICO	139	*umol/L	(25-110)
ARGINO-SUCCINICO	5	umol/L	(4-13)
HIDROXIPROLINA	9	umol/L	(5-30)
SERINA	129	umol/L	(60-180)
ASPARRAGINA	101	umol/L	(40-120)
GLICINA	250	umol/L	(105-350)
GLUTAMINA	578	umol/L	(300-675)
TAURINA	128	*umol/L	(30-125)
HISTIDINA	67	umol/L	(40-90)
CITRULINA	27	umol/L	(15-40)
TREONINA	84	umol/L	(60-175)
ALANINA	455	umol/L	(200-500)
ARGININA	98	umol/L	(50-170)
PROLINA	162	umol/L	(100-320)
TIROSINA	551	*umol/L	(35-100)
VALINA	262	umol/L	(150-325)
METIONINA	28	umol/L	(15-45)
CISTINA	15	umol/L	(15-55)
ISOLEUCINA	73	umol/L	(35-90)
LEUCINA	162	*umol/L	(70-160)
FENILALANINA	62	umol/L	(30-80)
TRIPTOFANO	52	umol/L	(30-70)
ORNITINA	105	*umol/L	(20-80)
LISINA	216	umol/L	(80-225)

Image 1: Tyrosine concentrations plasma

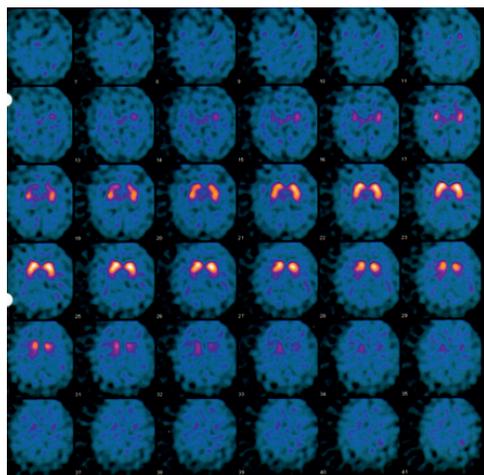


Image 3: DaT-SCAN SPECT

Conclusion: We present the first described case of hereditary tyrosinemia type 3 that was presented clinically as an atypical parkinsonism syndrome. We emphasize the importance of thinking in this disorder if we have a patient with essential tremor and parkinsonism symptoms, especially if they were started from infancy and there are other family members with these symptoms.

Disclosure: Nothing to disclose

EP2128

Depression and anxiety symptoms in dystonic patients

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Background and aims: To study depression and anxiety symptoms in patients with dystonia.

Methods: We treated 223 patients with dystonia (age 44.1±5.0 years, duration of diseases 9.3±0.49 years, the ratio of men and women 1.4:1). The control group consisted of 65 healthy volunteers. We used Hospital Anxiety Depression Scale (HADS), Beck and Spielberger scales and calculated the rate of reactive (situational) anxiety (RA) and personal anxiety (PA).

Results: The average anxiety index on HADS in patients with dystonia was 8.03±3.56, in control group - 2.56±2.08 (P>0.05). The average level of RA in patients with dystonia was 43.9±6.5 marks, in control group - 20.8±8.7 marks (P<0.01), the average level of PA in dystonia was 51.5±5.7 marks, in healthy volunteers - 43.6±8.1 marks (P<0.01). The average level of RA and PA in patients with dystonia means high anxiety. The average deression index on Beck scale in patients was 11.94±6.4 marks, in control group - 6.7±5.2 marks (P<0.05). Generally, 142 (63.7%) patients with dystonia and 8 (12.3%) healthy volunteers had symptoms of depression (P<0.01).

Conclusion: Patients with dystonia had a higher level of anxiety and depression. We have established a high level of PA which prevailed over RA on Spielberger scale. Psychologists and psychotherapists should be involved in treatment and rehabilitation of patients with dystonia.

Disclosure: Nothing to disclose

EP2129

Cancelled

EP2130

Use of the neuropsychiatric inventory to characterize the course of neuropsychiatric symptoms in progressive supranuclear palsy

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Background and aims: Several studies analyzed behavioral and neuropsychiatric symptoms of PSP and emphasized depression and/or apathy as the most prevalent. We aimed to determine the neuropsychiatric profile in our cohort of PSP patients and their dynamic changes over a follow-up period of one year.

Methods: A total of 59 patients were assessed at baseline, while 25 of them were accessible after one year of the follow-up. The detailed demographic and clinical interview was performed and appropriate motor and cognitive scales were applied. The presence of psychiatric symptoms was assessed using the Neuropsychiatric Inventory (NPI). In addition, depressive and anxiety symptoms, as well as apathy, were evaluated by the Hamilton Depression Rating Scale, the Beck Depression Inventory, Hamilton Anxiety Rating Scale, and the Apathy Scale, respectively. Statistical analysis of baseline data included both correlation and linear univariate and multivariate regression analyses. The value of changes of selected variables over one-year follow-up period, was quantified using the Wilcoxon signed ranks test. The level of these differences was calculated as an effect size.

Results: The most common symptoms were apathy and depression, which were also found to be the independent determinants of increased NPI total score in the longitudinal study. Apathy deteriorated most profoundly over the follow-up period.

Conclusion: Our study implied that apathy was a predominant feature of the behavior profile of PSP. Finally, the NPI seemed to be a sensitive measure of behavioral changes in PSP and could be included among potential outcome measures in future clinical trials in PSP.

Disclosure: This work has been funded by the Ministry of Education, Science and Technological Development Republic of Serbia (project no. 175090).

EP2131

Levodopa/carbidopa intestinal gel can improve both motor and non-motor experiences of daily living in Parkinson's disease: An open-label study

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Background and aims: Levodopa/carbidopa intestinal gel therapy (LCIG) can efficiently improve several motor and non-motor symptoms of advanced Parkinson's disease (PD). The recently developed Movement Disorder Society-sponsored Unified Parkinson's Disease Rating Scale (MDS-UPDRS) improved the original UPDRS making it a more robust tool to evaluate therapeutic changes. However, previous studies have not used the MDS-UPDRS and the Unified Dyskinesia Rating Scale (UDysRS) to assess the efficacy of LCIG. Our aim was to determine if the MDS-UPDRS and UDysRS could detect improvement in the experiences of daily living following 1-year LCIG treatment.

Methods: In this prospective, multicenter, open-label study, 34 consecutive patients undergoing LCIG treatment were enrolled. Patients were examined twice: prior to LCIG initiation and 12 months later. Impact of PD-related symptoms and dyskinesia was assessed by the MDS-UPDRS and UDysRS.

Results: Non-motor Experiences of Daily Living part of MDS-UPDRS improved from 20 (median, interquartile-range, IQR:14-23) to 16 points (median, IQR:12-20, $p=0.044$) and the Motor Experiences of Daily Living ameliorated from 24 (median, IQR:20-29) to 18 points (median, IQR:13-25, $p=0.025$). Health-related quality of life, measured by PDQ-39, also improved from 35.4 (median, IQR:26.9-50.3) to 27.0 (median, IQR:21.3-31.4) points ($p=0.003$). The total score of UDysRS decreased from 47 (median, IQR:36-54) to 34 (median, IQR:21-45) points ($p=0.003$).

Conclusion: As far as the authors are aware of, our paper is the first to evaluate the impact of LCIG on dyskinesia by the means of UDysRS. Changes in MDS-UPDRS and UDysRS confirm that LCIG treatment can efficiently improve experiences of daily living in advanced PD.

Disclosure: Our study was supported by the OTKA PD103964, and the Hungarian Brain Research Program - Grant No. KTIA_13_NAP-A- II/10 government-based funds, NK was supported by the New National Excellence Program of the Ministry of Human Capacities, Hungary.

parameters than bilateral stimulation, but right and left-sided stimulation still need to be further examined with a detailed analysis of the electrode positions.

Disclosure: Nothing to disclose

EP2132

Quantitative assessment of gait parameters in Parkinsonian patients treated with bilateral subthalamic stimulation

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Background and aims: The effects of bilateral subthalamic stimulation (STN-DBS) on gait in Parkinson's disease varied in previous studies. Our aim was to analyse how bilateral STN-DBS influences the kinematic parameters of gait in Parkinson's disease during an instrumented timed up-and-go (ITUG) test.

Methods: Thirteen Parkinsonian patients treated with STN-DBS performed the ITUG-test in both OFF (NON), left ON (LON), right ON (RON) and both ON (BON) stimulation conditions in randomized order, in medication OFF stage. Six Opal monitors (APDM Inc.) consisting of a 3-axis accelerometer and gyroscope were placed on the two wrists and ankles, trunk and chest. Mobility Lab software (APDM Inc.) was used for data analysis. The Wilcoxon signed rank test was performed to compare gait parameters in the conditions.

Results: The total duration of the ITUG-test, stride length, and stride velocity improved in BON compared to NON state (Table1). The gait rhythmicity and the time proportion of double support were similar in the two conditions. Bilateral stimulation significantly improved the trunk velocities during gait, the turning duration, and the turn peak velocity. The RON – but not LON, condition improved the parameters of turning. Turn-to-sit time was shorter in BON than in NON state, but their difference was not significant.

	Total duration (sec)	Stride Length (% of Stride)	Stride Velocity (% of 2.0m/sec)	Cadence (steps/min)	Double Support (% of gait cycle time)	Turning Duration (sec)	Turning Peak velocity (degree/sec)	Turn-to-sit Time (sec)
NON median(IQR)	30(6,3)	68(12,9)	61(11,7)	108(19)	23(3,7)	2,7(1,29)	129(39,6)	4,1 (1,74)
BON median(IQR)	20(4,4)	72(6,9)	65(12,7)	106(14)	21(5,1)	2,2(0,55)	158(32,5)	3,7(0,96)
level of sign.- p	0,02	0,009	0,007	NS	NS	0,023	0,013	0,055

Table 1. Gait parameters during ITUG test in BON (both ON) and NON (both OFF) states

Table 1.

Conclusion: Many gait and turning parameters improved with bilateral stimulation consistently with previous findings. Unilateral stimulation had lower effects on most

EP2133

Paroxysmal painful dystonia of leg muscles in vascular parkinsonism

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Background and aims: Vascular parkinsonism (VP) is a nosology the clinical picture of which is not clearly delineated. Objective of our investigation was to study all the clinical manifestations of the patients with VP.

Methods: 12 patients (5 women/7men, aged 65-80 years) were investigated using UPDRS, Tinetti scale and MoCA. Diagnosis of VP was based on the presence of multiple lacunes on brain MRI along with lower-body parkinsonism. All the patients were receiving L-Dopa (500-1000 mg/day).

Results: In all patients most prominent symptom was gait disturbance- start hesitation, freezing and festination. There was prominent hypokinesia and rigidity in legs as opposed to hands. 7 patients had rigidity of axial muscles. 5 patients had mild postural tremor in hands. There was no gaze palsy detected. 10 patient have mild cognitive impairment. Response to L-Dopa was poor in all the cases. All women patients experienced attacks of severe and very painful dystonic spasm of leg muscles with enormous hypertonia of leg extensors, so that it was impossible to perform passive flexion. Spasm lasted from 10 min up to 1 hour and repeated several times a day and at night. No such phenomena was observed in male patients. In all 5 patients gabapentin 900-1600 mg/day effectively reduced attacks of painful dystonia.

Conclusion: Painful leg dystonia can be regarded as a characteristic symptom of vascular parkinsonism. Dystonic attacks are not related to L-Dopa wearing-off and can be effectively controlled with gabapentine.

Disclosure: Nothing to disclose

Movement disorders 4

EP2134

A novel SCN4A N440K transgenic zebrafish model of human nondystrophic myotonia

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Background and aims: The present study aimed to gain insight into the pathophysiological basis of nondystrophic myotonia and the phenotypic heterogeneity of the human SCN4A(hSCN4A) N440K mutation.

Methods: A novel transgenic zebrafish model of human nondystrophic myotonia was generated and validated using electromyography (EMG) and behavioral tests.

Results: The hSCN4AN440K mutant zebrafish exhibited both exercise- and cold-induced myotonia, as determined by the typical EMG finding of myotonic discharges with dive-bomber sound and a typical “dive-bombing behavior”, respectively. The mutant fish achieved lower values in the parameters tested (mean velocity and distance moved, and time spent and number of visits in zones) than control fish. No consistent pattern indicative of the warm-up phenomenon or paramyotonia was observed.

Conclusion: We report herein the first zebrafish model of exercise- and cold-induced human nondystrophic myotonia. The phenotypic heterogeneity of hSCN4A N440K might not be attributed to the mutation alone. Our results provide insight into the pathophysiology of myotonia in sodium channelopathy and could be used for exploring a new therapeutic avenue.

Disclosure: This work was in part funded by a grant from the Korea Health 21 R&D Project, Ministry of Health, Welfare & Family Affairs, Republic of Korea (A100402).

EP2135

Cerebrospinal fluid biomarkers in a cohort of p.A53T SNCA mutation carriers: Correlation with clinical phenotype

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Background and aims: The p.A53T point mutation in the α -synuclein gene is a rare cause of autosomal-dominant Parkinson's disease (PD). The classical phenotypes include PD, PD with dementia (PDD), or dementia with Lewy bodies. However, data available on cerebrospinal fluid (CSF) biomarkers in p.A53T carriers are largely lacking. Our study aims to measure CSF levels of beta-amyloid1-42, total-tau, and phospho-tau181, in A53T PD and non-manifesting carriers.

Methods: A total of 9 CSF samples were analyzed: 7 A53T PD patients and 2 asymptomatic p.A53T carriers. All participants underwent a detailed diagnostic assessment, including clinical (MDS-UPDRS), neuropsychological investigations (MOCA, GDS), brain MRI scans and CSF biomarker analysis.

Results: The phenotype of symptomatic carriers was variable, with 3 patients manifesting typical motor parkinsonian symptoms without cognitive involvement, 2 PDD patients with initial motor symptoms and later onset cognitive decline, and 2 patients exhibiting an atypical frontotemporal dementia (FTD)like phenotype prior to parkinsonism onset. CSF A β 42 levels were marginally decreased only in 2 PDD patients. CSF total-tau level was elevated in both FTD phenotype patients, but was normal in the remaining A53T carriers (5 symptomatic/2 asymptomatic), regardless of their cognitive profile. Phospho-tau181 were within normal limits. Brain MRI scans were normal in all subjects, with the exception of the 2 FTD phenotype patients who demonstrated fronto-temporo-parietal atrophy.

Conclusion: p.A53T carriers demonstrate an heterogeneous CSF biomarker profile which could correlate with their variable degree of motor and cognitive deterioration. Further investigations are required to test the predictive performance of CSF biomarkers in this rare genetic PD cohort.

Disclosure: Nothing to disclose

EP2136

Middle cerebellar peduncle lesions – various tremor characteristics

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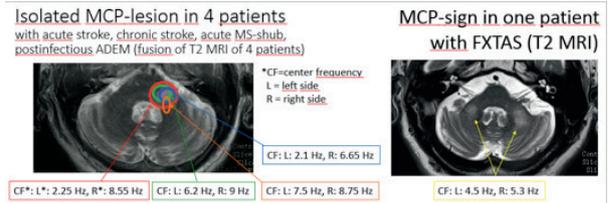
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Background and aims: Recent studies suggest that alterations of the cerebello-thalamo-cortical network are responsible for tremorogenesis in essential tremor. The middle cerebellar peduncle (MCP) represents a key connection in this network as it conveys afferent fibers from the cerebral cortex to the cerebellum. We report a case series of patients with lesions of the middle cerebellar peduncle (MCP) having different tremor characteristics.

Methods: We analyzed quantitatively the tremor of 116 patients with brainstem and/or cerebellar lesions and here we report the results of 5 patients with MCP lesion of different causes (1 patients with acute stroke, 1 with subacute stroke, 1 with multiple sclerosis, 1 with post-infectious ADEM, and 1 patient with fragileX tremor-ataxia syndrome (FXTAS)). Tremor was measured by biaxial accelerometry. Center frequency, frequency dispersion and tremor intensity were calculated. In 4 patients, control measurements were performed to assess the evolution of tremor. Detailed analysis of the MRI-data were performed by a neuroradiologist.

Results: Pathologic tremor was detected in 3/5 patients (60%). Tremulous patients had acute stroke/MS-shub or FXTAS. Their tremor had low intensity, low center-frequency (2 Hz), whereas tremor of FXTAS-patient had higher intensity and a center-frequency of 5 Hz. Frequency dispersion was low in both categories. Acute patients presented a complete tremor recovery in cca. 4 weeks, whereas the FXTAS patient's tremor worsened.



Patients' MRI

Conclusion: Our results show that the location of the lesion does not explain the mechanism of tremorogenesis and tremor characteristics. The pathomechanism of the lesion might influence tremor frequency and evolution.

Disclosure: Nothing to disclose

Patient ID	Signs and symptoms	Diagnosis	Side of the lesion	Tremor frequency on the left side	Tremor frequency on the right side
ADV1	gait-evoked myasthus to the right, dysarthria, scanning speech, left-sided dysidiadochomesia and dysmetria, truncal ataxia, gait ataxia	multiple sclerosis	left	2.25 Hz*	8.55 Hz
KAS7	gait ataxia, ataxia in the right lower limb	post-infectious ADEM	both sides	7.5 Hz	8.75 Hz
KaTSO	horizontal nystagmus to the right, diplopia, light dysarthria, left-sided limb ataxia, severe truncal ataxia, gait ataxia, deviation to the left	acute ischaemia	left	2.1 Hz	6.65 Hz
BI4	diplopia, left-sided dysidiadochomesia, unure in Romberg-position	subacute ischaemia	left	6.2 Hz	9 Hz
RDVG	intention tremor, rigor in both arms, left-sided dysidiadochomesia, gait ataxia	fragile X tremor ataxia syndrome (with MCP-lesion)	both sides, with left preponderance	4.5 Hz	5.3 Hz

*red colour denotes pathologic values

Patients' data

EP2137

The mutual relationship of bilateral subthalamic stimulation impact on the non-motor and motor symptoms in Parkinson's disease - an open prospective pilot study

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Background and aims: There are numerous studies which have documented significant improvement in motor symptoms and quality of life in patients with Parkinson's disease after deep brain stimulation of the subthalamic nucleus (STN-DBS). However, relatively little is known about the effects STN-DBS on non-motor symptoms.

Methods: 24 patients with advanced PD who underwent STN-DBS were followed up in open prospective study. They were examined and assessed, using dedicated rating scales preoperatively and at 1 and 4 months following the implantation to determine changes in overall motor and non-motor symptoms.

Results: STN-DBS in patients with PD at Month 1 significantly reduced PDQ-39 score ($p=0.018$) and SCOPA-AUT score ($p=0.002$), but 4 months after implantation they were again increased. NMSS improved significantly at Month 1 ($p=0.0001$) and at Month 4 remained significantly lower than before stimulation ($p=0.036$). There was no significant difference in PDSS between baseline and Month 1 after DBS, but we can see a significant increase in PDSS at Month 4 ($p=0.026$). The UPDRS-MDS Part III scores show a significant improvement 1 month ($p=0.0006$) and also 4 months after DBS ($p<0.0001$). At Month 1 as well as at Month 4, DBS resulted in no significant changes in FSFI and IIEF. Impulse control disorder was present in only 4 patients, so we do not list the results as they cannot be considered relevant.

Conclusion: STN-DBS in patients with advanced Parkinson's disease clearly improves not only motor symptoms, but also several domains of non-motor functions, namely sleep, autonomic functions and quality of life.

Disclosure: This work was supported by the grant IGA UPOL-LF-2016-033, grant AZV MZ CR Nr. 15-32715A.

EP2138

Cancelled

EP2139

Clinical manifestation of the Huntington's disease in Belarus

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Background and aims: Huntington's disease (HD) is an inherited, progressive disease, characterized by combination of motor, cognitive and psychiatric symptoms. It is caused by an expanded trinucleotide CAG repeats in the HTT gene.

Methods: We performed neurological examination of 65(100%) patients with HD. 45(69%) subjects were genetically tested for CAG repeats in the HTT gene.

Results: Age of the patients was 21 - 69 (47 ± 9.3) years old; the age of the onset of HD was 18 - 65 (41.5 ± 8.1). 56(85%) patients had positive family history and 9(15%) didn't know all information about their relatives. Neurological examination revealed choreiform hyperkinesia and cognitive impairment in 65(100%) patients. Dystonic hyperkinesia was observed in 41% cases; hypotonia in upper and lower extremities in 40%; coordination disturbances in 37%, pyramidal signs in 29%, dysarthria in 17%. 2(3%) patients had predominance of marked cognitive impairment and 1(1.5%) akinetic-rigid syndrome in the onset of HD. Juvenile form was diagnosed in 1(1.5%) patient. The age of the onset was 18 years old; clinical signs included predominance of marked cognitive impairment and cerebellar ataxia, light choreiform hyperkinesia.

Genetic testing of 45 HD subjects revealed expansion of CAG repeats from 39 to 66 in the HTT gene.

Conclusion: The most of patients (95%) had typical neurological manifestation of HD. Only 4(6.1%) subjects presented atypical signs with difficulty of diagnostics. Significant reverse correlation between the age of the onset of HD and the number of trinucleotide CAG repeats in the HTT gene was determined ($r=-0.846$, $p<0,01$).

Disclosure: Nothing to disclose

EP2140

Globus pallidus internus deep brain stimulation in the treatment of generalized dystonia

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Background and aims: Deep brain stimulation (DBS) is well studied in the treatment of primary generalized dystonia and was approved by FDA in 2003 as a humanitarian device exemption. DBS has been also used in the experimental treatment of secondary dystonia.

Methods: We retrospectively reviewed all cases of generalized dystonia treated with pallidal DBS from December/2005 until January/2016. We collected and analysed clinical data.

Results: We selected 14 patients, 6 with primary and 8 with secondary dystonia. The median of improvement in Burke-Fahn-Marsden (BFM) score at 12 months was 59.9% (22.9%-90.0%) in primary and 43.6% (18.0%-54.0%) in secondary dystonia. The median of improvement in Dystonia Disability Scale (DDS) at 12 months was 48.1% (33.3%-85.2%) in primary and 20.3% (12.0%-50.0%) in secondary dystonia. 6 patients have long-term follow-up (>5 years). 3 of them have primary dystonia and sustained benefit in BFM (55%-90%) and DDS (50%-85%). The other 3 patients have secondary dystonia and heterogeneous results: 1 with PANK2 had sustained benefit at 5 years (BFM: 17%; DDS: 18%), 1 with perinatal anoxia improved after neurostimulation disconnection and 1 with iatrogenic dystonia from neuroleptics had improvement of 96% in BFM and 100% in DDS.

Conclusion: Our patients with generalized primary dystonia, similar to the existent literature results, had good response to DBS, sustained at long-term. Secondary dystonia group is heterogeneous, had lower median benefit and highly variable results at long-term. However, some of these patients had improvements in quality of life not always well translated by the existent formal scores.

Disclosure: Nothing to disclose

EP2141

Dopamine D2 receptor mediated neuroprotection in a LRRK2 genetic model of Parkinson's disease

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Background and aims: Parkinson's Disease (PD) is a neurodegenerative disease in which genetic and environmental factors are synergistically involved. Lrrk2 gene mutations are responsible for the majority of inherited cases of PD. We investigated the alterations of striatal medium spiny neurons (MSNs) activity and the neuronal vulnerability to mitochondrial dysfunction in a genetic mouse model carrying the G2019S knock-in (KI) mutation. **Methods:** Excitatory postsynaptic currents (EPSCs) were recorded by patch-clamp experiments. Striatal dopamine (DA) release was measured by constant potential amperometry. Neuronal vulnerability to rotenone, a complex I inhibitor, was tested by measuring the progressive reduction of striatal field potential amplitude (FPA).

Results: In KI mice, we showed reduced striatal DA levels by 49% ($p < .05$). We found that the DA-D2 receptor agonist quinpirole markedly reduced spontaneous (31%, $p < .05$) and evoked EPSCs (38%, $p < .05$) in KI but not in control mice. The CB1-endocannabinoid receptor antagonist blocked this effect. The rotenone-induced loss of the FPA was markedly enhanced in KI compared to control mice (24%, $p < .05$). This detrimental effect was counteracted only in KI mice by the application of quinpirole, through the inhibition of the cAMP/PKA pathway.

Conclusion: The G2019S mutation is associated with an altered striatal DA and glutamate transmission. In KI mice, the DA-D2R activation was able to reduce striatal glutamate release through a CB1R-dependent mechanism and limited rotenone-induced neuronal dysfunction, via the inhibition of cAMP/PKA intracellular pathway. Neuroprotective strategies targeting DA-D2R could counteract the synergistic effect of genetic and environmental predisposing factors in patients carrying this mutation.

Disclosure: This study was supported by Ministero della Salute (RF-2011-02349806) "Mitochondrial targeting in LRRK2-associated parkinsonism (PARK8)"

EP2142

Hereditary spastic paraplegia type 11 and 22q11 duplication syndrome in a single family

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Background and aims: Hereditary spastic paraplegia (HSP) type 11 is a rare autosomal recessive form of complex HSP with thin corpus callosum. The 22q11 duplication syndrome is an autosomal dominant disorder, characterized by developmental delay, intellectual disability, dysmorphias and wide intrafamilial phenotypic variability.

Methods: Case report.

Results: The index case is a 36-year-old man with a term birth and normal developmental milestones during childhood with early learning difficulties. At the age of 23, a rapid progressive spastic paraparesis appeared. Brain and cervical MRI were both normal. Neither of his nonconsanguineous parents showed similar symptoms. They had 10 children. One older female sibling (patient 2) also had paraparesis, more severe, with younger age of onset (4 years) and by the age of 15 she needed walking assistance. Brain MRI revealed white matter changes with thin corpus callosum. Another female sibling (patient 3) had intellectual disability with learning difficulties, but normal motor skills. On examination, the mother (patient 4) and three children had a dysmorphic appearance with hypertelorism and low implantation of ears. Genetic studies revealed a pathological variant in SPG11 gene in the index case and patient 2; and a pathological variant in chromosome 22 (22q11 duplication) in the index case, patients 2, 3 and 4.

Conclusion: The occurrence of two rare inherited conditions (one autosomal dominant and other autosomal recessive) in the same family is, beyond unlikely, responsible for phenotypic variability and also for diagnostic challenge.

Disclosure: Nothing to disclose

EP2143

New possibilities of the transcranial sonography in Parkinson's disease patients

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Background and aims: Transcranial sonography (TCS) is an inexpensive non-invasive safe method used for early diagnosis of Parkinson's disease (PD). We aimed to explore TCS to evaluate cerebral atrophy, accompanied by cognitive decline in PD patients.

Methods: 100 patients with PD underwent TCS and neuropsychological evaluation included Mini-Mental State Examination, Frontal Assessment Battery, Parkinson's Disease-Cognitive Rating Scale.

Results: According to neuropsychological testing PD patients were divided into three groups – cognitive-intact, with mild cognitive impairment (MCI), and with dementia. These groups differed on the following TCS parameter: substantia nigra (SN) hyperechogenicity (Kruskal-Wallis $H=15,61; p<0.001$), third ventricle width ($H=23,92; p<0.001$), and frontal horns of the lateral ventricle width ($H=9,41; p=0.009$). Pairwise comparisons revealed that cognitive-intact group differed ($p<0.001$) from the MCI group and from dementia group in an average size of SN hyperechogenicity and third ventricle width. In addition, a cognitive-intact group differed from dementia group in frontal horns of the lateral ventricle width ($p=0.003$). The MCI group differed from dementia group only in third ventricle width ($p=0.016$). Thus, we concluded that only the third ventricle width is a good marker of cognitive impairment in PD patients. We established that the optimum threshold separating III ventricle width allows detecting atrophic changes in the brain, accompanied by cognitive impairment calculated with ROC-analysis was ≥ 7.4 mm, $AUC=0,78$ (95% CI 0.68-0.89), $p=0.001$ testified that identified neuroimaging marker has a good informative value.

Conclusion: These findings suggest that TCS may be sensitive to cognitive changes in PD with optimal threshold division III ventricle width of 7,4 mm.

Disclosure: Nothing to disclose

EP2144

Acquired hepatocerebral degeneration - A metabolic acquired movement disorder

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Background and aims: Acquired hepatocerebral degeneration is a debilitating neurological disorder characterized by parkinsonism, ataxia and other movement disorders, which may accompany various forms of advanced liver disease.

Results: 58-year-old man with past medical history of nonalcoholic steatohepatitis with portal hypertension, progressively developed apathy, bradyphrenia, mild cognitive impairment and language disorder. Neurological examination revealed a palpable spleen, dysarthric speech, left resting tremor, asymmetric rigidity and a buco-lingual chorea. Blood test revealed an elevated AST, ALT, GGT and ammonia. Investigation also included a Brain CT and EEG that were normal. The MRI demonstrated increased T1 signal within the pallidal nuclei which may be associated with a toxic-metabolic disorder. The patient's diagnosis was an acquired hepatocerebral degeneration and he refused liver transplantation.

Conclusion: Acquired hepatocerebral degeneration is an important differential diagnosis of movement disorders with MRI T1 hyperintensities in the basal ganglia. Portosystemic shunting leads to accumulation of toxins such as ammonia that are bypassing the first-pass elimination by the liver. Evidence suggests manganese plays a crucial role in the pathogenesis of this disease. They are no proven pharmacological therapies, although liver transplantation is helpful in some patient.

Disclosure: Nothing to disclose

EP2145

The identification of molecular-genetic background of familial atypical parkinsonism in “Hornacko”, a specific region of south-eastern Moravia, Czech Republic

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Background and aims: Increased prevalence of parkinsonism was detected in a small region of the Czech Republic. Three large pedigrees with autosomal-dominant inheritance patterns of parkinsonism were identified. The aims of the study were to assess the genetic background of atypical familial neurodegenerative parkinsonism.

Methods: Molecular genetic examinations were performed in 12 clinically positive probands. Coding sequences, exon/intron regions and 5'/3'UTR sequences of ADH1C, ATP13A3, EIF4G1, FBXO7, GBA+GBAP1, GIGYF2, HTRA2, LRRK2, MAPT, PARK2, PARK7, PINK1, PLA2G6, SNCA, UCHL1, and VPS35 genes were tested with a massive parallel sequencing method using Ion Torrent technology and confirmed by Sanger sequencing. In total, 93% of gene sequences were covered.

Results: 31 rare heterozygous variants have been identified. The most interesting variants (PhyloP score ≥ 2 and/or missense variants) included: one variant in coding sequence - c.143C>T in ADH1C gene, one variant in coding sequence - c.689A>G in MAPT gene, one variant in UTR-3 region sequence - c.*77G>T in SNCA gene, one variant in exon - c.1180C>T in PARK2 gene, one variant in coding sequence - c.344A>T in PINK1 gene, three exon variants - c.2167A>G, c.6241A>G, c.4541G>A in LRRK2 gene, one variant in coding sequence - c.3662C>T in GIGYF2 gene, one exon variant - c.1027C>T in PLA2G6 gene and one variant in coding sequence - c.3706C>G in EIF4G1 gene.

Conclusion: It seems that several molecular-genetic factors play role in the genetic background of this newly detected atypical familial neurodegenerative parkinsonism.

Disclosure: This work was supported by Ministry of Health of the Czech Republic grant Nr. 15-32715A, MH CZ – DRO (FNOL 00098892) – 2016 and IGA-LF-2016-026.

EP2146

Atypical phenotypes of CADASIL: Two cases

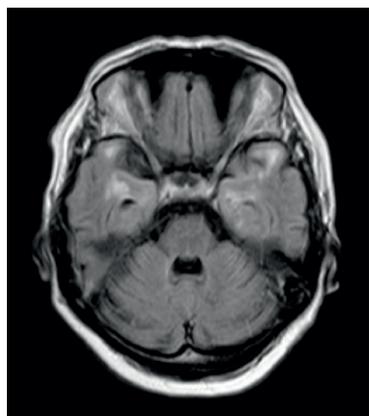
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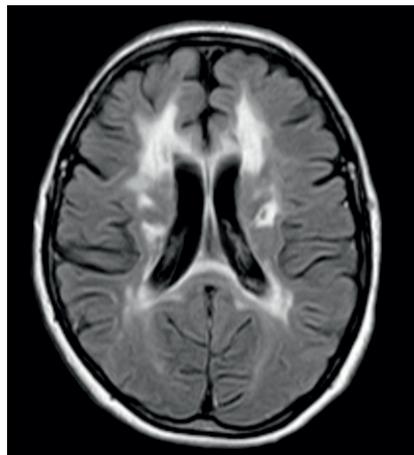
Background and aims: Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is central nervous system inherited disease that is caused by NOTCH3 gene mutation. It is characterized by headaches, strokes, dementia. Specific magnetic resonance imaging (MRI) signs are lacunar infarctions, focal lesions of temporal poles, capsula externa, periventricular and subcortical areas and diffuse white matter changes. Rarely CADASIL begins with unusual symptoms. We hereby present two clinical cases of the disease manifested by movement disorders.

Methods: We examined two female patients (A, 79 y.o., B, 47 y.o.) using neurologic and neuropsychological testing, brain MRI, NOTCH3 gene sequencing.

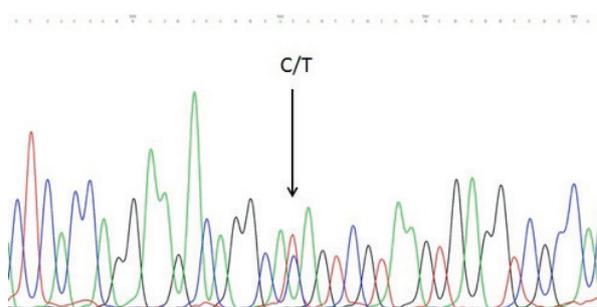
Results: Both patients complained of tremor and gait instability. No factors for stroke were revealed. Family history: A-hereditary untainted; B - father died of repeat stroke. Neurologic examination: A-broken pursuit eye movements, vocal tremor, head and body titubation, proximal arm tremor, intension tremor and coordination disturbances in arms, ataxic gait; B-euphoria, judgement declined, mild rigidity in left hand, wrists postural tremor (S>D), intension tremor and coordination disturbances in arms, ataxic gait. Montreal Cognitive Assessment and Frontal Assessment Battery revealed cognitive decline and frontal dysfunction in both cases. Neurodegenerative process was considered in both cases, so the brain MRI were performed. In both cases classical CADASIL signs were found (fig.1, 2). NOTCH3 gene sequencing revealed mutations in the 4th exon of the gene: A - R207C (fig.3); B - C222Y.



Axial T2-FLAIR weighted image shows temporal poles hyperintensity



Axial T2-FLAIR weighted image shows confluent lesions of deep white matter and periventricular area



Pathogenic R207C mutation in the NOTCH3 gene.

Conclusion: This report emphasizes that CADASIL is clinically heterogeneous and should be considered in the study of patients with atypical movement disorders.

Disclosure: Nothing to disclose

MS and related disorders 3

EP2147

The role of neutrophil-to-lymphocyte ratio in multiple sclerosis and optic neuritis

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Background and aims: This study evaluates the significance of the blood neutrophil-to-lymphocyte ratio (NLR) in the different courses of multiple sclerosis (MS); relapsing-remitting MS (RRMS), secondary progressive MS (SPMS), primary progressive MS (PPMS) and optic neuritis (ON). The NLR is measured in relation to relapse and remission and Expanded Disability Status Scale (EDSS).

Methods: 382 patients suffering from RRMS (n=138), SPMS (n=30), PPMS (n=55), CIS (n=19) or ON (n=140) and 813 healthy controls (HC) were included. Complete blood count, demographic, and clinical data from MS patients were evaluated retrospectively. The NLRs were calculated and compared for all participants by Student's t-test. Logistic regression models were constructed for EDSS \geq 4,0 as outcome and age, gender, NLR, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), erythrocyte distribution width (ERYDRW) and disease duration as predictor variables.

Results: The NLR is significant higher ($p < 0.001$) in MS and ON patients compared to HC. Patients in relapse had a significant higher NLR ($p < 0.005$) than patients in remission, but no difference in the CRP, ESR, ERYDRW and EDSS. No variance in NLR was found between RRMS and progressive MS patients and neither between SPMS and PPMS patients. No significance was found between any of the predicting variables and an EDSS score \geq 4.0.

Conclusion: MS and ON patients have a significantly higher NLR than HC, indicating the occurrence of chronic inflammation. NLR may be a marker of disease activity, because of the significantly higher NLR in patients with relapse compared to patients in remission. This needs confirmation in future trials.

Disclosure: Nothing to disclose

EP2148

Adherence comparison in multiple sclerosis in a real-world setting: New oral versus classic injectable disease modifying treatments

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Background and aims: New oral disease modifying therapies (oDMT) for relapsing remitting multiple sclerosis (RRMS) are available. The aim was to assess patient adherence to oDMT: dimethyl fumarate (DMF) and teriflunomide (TE) in comparison with classic injectable therapies (iDMT).

Methods: RRMS patients switched from iDMT (interferon-beta-1a/1b/glatiramer acetate) to new oDMT between June 2015 and March 2016 in Hospital Alvaro Cunqueiro were recruited. Adherence, measured by medication possession ratio (MPR) and expressed in%, was compared for oDMT versus iDMT. Adherent patient was considered if $MPR \geq 90\%$.

Results: 38 patients were switched from iDMT to DMF (n=20) or TE (n=18). Women: 87.8%, mean age (\pm SD): 39.2 ± 8.5 years; mean disease duration: 6.0 ± 5.0 years; median EDSS (range): 2[0-6.5]; annualized relapse rate (ARR): 0.7 ± 0.8 . 66.7% patients were switched from interferon-beta and 33.3% from GA. Prior mean treatment duration (SD): 423.4 ± 167.2 days. The main reasons for change were inefficacy (59.4%) and intolerance (40.6%). 5 patients stopped oDMT (1 patient due to pregnancy, 3 patients due to GI intolerance and 1 due to lymphopenia). Mean oDMT duration: 166.5 ± 59.3 days. MPR to iDMT=85.2% vs. MPR to oDMT=98.1% ($p < 0.001$). No MPR differences between oDMT were observed. iDMT adherence among patients who switched to TE was 83.4% and 85.7% in patients switched to DMF ($p > 0.05$). Adherence $> 80\%$ was observed in 70% of patients on iDMT and in 100% on oDMT.

Conclusion: Patients on oDMT present better adherence than those previously treated with iDMT. These changes may have an important impact on disease control. More real-world data are necessary to evaluate long-term adherence to oDMT.

Disclosure: Nothing to disclose

EP2149

Spinal cord lesions are frequently asymptomatic in relapsing remitting multiple sclerosis. A retrospective MRI survey

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Background and aims: Spinal cord (SC) lesion load is well known as a negative prognostic factor in multiple sclerosis (MS). Nevertheless, there is no consensus about MRI follow-up, mainly because new SC lesions (SCLs) are thought to be more likely symptomatic than brain ones. The aim of the present study was to investigate the impact of asymptomatic active SCLs, defined as new/enlarging T2 or gadolinium positive (Gd+), on SC MRI activity in a cohort of MS patients.

Methods: We retrospectively investigated all available SC MRI scans of clinically isolated syndrome and relapsing remitting (RR) MS patients referred to a single Italian MS centre, analysing those with active SCLs, both symptomatic and asymptomatic, collecting also clinical data since previous SC MRI or disease onset in case of first examination. Brain MRI data were also included.

Results: We analysed a total of 340 SC MRI scans from 230 patients. We found asymptomatic active SCLs in 31.2% of scans. At multivariate analysis, compared to symptomatic, asymptomatic active SCLs were associated with an older age at disease onset (34.0 ± 10.37 vs 31.0 ± 9.99 yrs, $p=0.039$), more frequent RR course (96.2 vs 92.7%, $p=0.037$) and sovratentorial location at onset (14.2 vs 6%, $p=0.027$), lower EDSS score (1.6 ± 0.88 vs 2.4 ± 1.29 , $p=0.001$), less relapses since previous SC MRI or disease onset (1.1 ± 1.13 vs 2.1 ± 1.78 , $p=0.003$) and less new/enlarging T2 SCLs (1.6 ± 1.07 vs 2.1 ± 1.54 , $p=0.043$).

Conclusion: A consistent part of active SCLs seems to remain asymptomatic, suggesting the need of a regular SC MRI follow-up.

Disclosure: Nothing to disclose

EP2150

Low rate of conversion from relapsing-remitting MS to secondary progressive MS through 6 years among patients who received alemtuzumab in CARE-MS I and II

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Background and aims: Delaying conversion from relapsing-remitting MS (RRMS) to secondary progressive MS (SPMS) is an important MS treatment goal. In an MSBase patient cohort (17,356 MS patients; median baseline disease duration 3.8 years; median 5.8-year follow-up), 18% of all patients converted to SPMS using a recently developed SPMS definition based on EDSS scores and relapses. The aim of this analysis was to determine the rate of conversion to SPMS among well-defined cohorts of patients with active RRMS who were either treatment-naive (CARE-MS I [NCT00530348]) or had inadequate response (≥ 1 relapse) to prior therapy (CARE-MS II [NCT00548405]); extension study (CAMMS03409 [NCT00930553]).

Methods: Patients received 2 courses of alemtuzumab 12 mg (baseline: 5 consecutive days; 12 months later: 3 consecutive days) in CARE-MS I or CARE-MS II, and in the extension as-needed alemtuzumab for relapse/MRI activity, or another disease-modifying therapy per investigator discretion. We performed a pooled analysis to determine conversion from RRMS to SPMS in alemtuzumab-treated patients through 6 years. The definition of SPMS onset was as published by Lorscheider et al. (Brain 2016;139:2395-405).

Results: Of 811 CARE-MS I/II RRMS alemtuzumab-treated patients (median baseline disease duration 2.8 years), 669 (82.5%) remained on study through Year 6, and 20/811 (2.5%) met the definition of SPMS through 6 years using progression confirmation of ≥ 3 months (12/811 [1.5%] over ≥ 6 months). Additional sensitivity analyses, similar to those reported previously by Lorscheider et al, showed consistent results.

Conclusion: A low proportion of alemtuzumab-treated patients progressed to SPMS through 6 years.

Disclosure: Sanofi and Bayer HealthCare Pharmaceuticals

EP2151

Vitamin D status predicts brain MRI activity in patients with clinically isolated syndrome

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Background and aims: Lower Vitamin D levels have recently been associated with increased clinical activity among the patients with multiple sclerosis (MS) or clinically isolated syndrome (CIS). Aim of this study is to determine if vitamin D status is associated with developing new T2 lesions or contrast enhancing T1 lesions on brain magnetic resonance imaging (MRI) in the patients with CIS and could contribute to early conversion to MS.

Methods: A longitudinal prospective study was conducted on forty-three Egyptian patients diagnosed as CIS according to McDonald's criteria (2010). The patients underwent detailed clinical assessment, evaluation of MRI brain including the number of new hyperintense T2 lesions, new gadolinium enhancing T1 lesions and 25-hydroxyvitamin D levels at baseline and after 1 year follow up.

Results: The CIS patients that converted to MS showed higher number of new T2 lesions than non converters ($p < 0.001$) after 1 year follow up. There was a significant negative correlation between 25 hydroxyvitamin D level and MRI T2 lesions number ($r = -0.38$, $p = 0.01$) and gadolinium T1 lesions ($r = 0.37$, $p = 0.02$). It was shown that the CIS patients that had lower levels of 25-hydroxyvitamin D below 7.1 ng/ml were at higher risk for developing new T2 brain lesions at MRI brain with sensitivity (100%) and specificity (91.3%).

Conclusion: Vitamin D deficiency could be associated with MRI brain activity and early predict conversion of CIS patients to MS.

Disclosure: Nothing to disclose

EP2152

Cancelled

EP2153

Hypothalamic damage in multiple sclerosis correlates with disease activity, disability, depression and fatigue

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Background and aims: Disturbances of the hypothalamo-pituitary (HPA) axis are supposed to modulate activity of multiple sclerosis (MS). We hypothesised that the extent of HYP damage may determine severity of MS and may be associated with the disease evolution. We suggested fatigue and depression may depend on the degree of damage of the area.

Methods: 33 MS patients with relapsing-remitting and secondary progressive disease, and 24 age and sex-related healthy individuals (CON) underwent 1H-MR spectroscopy (1H-MRS) of the hypothalamus. Concentrations of glutamate+glutamin (Glx), cholin (Cho), myoinositol (mIns), N-acetyl aspartate (NAA) expressed as ratio with creatine (Cr) and N-acetyl aspartate (NAA) were correlated with markers of disease activity (RIO score), Multiple Sclerosis Severity Scale (MSSS), Depressive-Severity Status Scale (SDSS) and Simple Numerical Fatigue Scale (SNFS).

Results: Cho/Cr and NAA/Cr ratios were decreased and Glx/NAA ratio was increased in MS patients vs CON. Glx/NAA, Glx/Cr, and mIns/NAA were significantly higher in active (RIO 1-2) vs non-active MS patients (RIO 0). Glx/NAA and Glx/Cr correlated with MSSS and fatigue score, and Glx/Cr with depressive score of MS patients. In CON relationships between Glx/Cr and age, and Glx/NAA and fatigue score were inverse.

Conclusion: Our study provides the first evidence about significant hypothalamic alterations correlating with clinical outcomes of MS, using 1H-MRS. The combination of increased Glu or mIns with reduced NAA in HYP reflects whole-brain activity of MS. In addition, excess of Glu is linked to severe disease course, depressive mood and fatigue in MS patients, suggesting superiority of Glu over other metabolites in determining MS burden.

Disclosure: This work has been supported by Project APVV-14-0088/2014 and Grant VEGA 1/0287/16.

EP2154

ASCLEPIOS I and II: Adaptive design of two parallel phase 3 studies in relapsing multiple sclerosis

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Background and aims: In a phase 2b study, subcutaneously administered ofatumumab significantly reduced the cumulative number of new gadolinium-enhancing lesions during weeks 4–12 by $\geq 90\%$ versus placebo in patients with relapsing multiple sclerosis (RMS). Here, we present the adaptive design features of the two ongoing, double-blind/double-dummy, identical design phase 3 studies of ofatumumab in RMS (ASCLEPIOS I [NCT02792218] and ASCLEPIOS II [NCT02792231]).

Methods: Patients (N=900, each trial) will be randomised to subcutaneous ofatumumab 20mg every 4 weeks or oral teriflunomide 14mg once daily. The primary endpoint is to demonstrate the superiority of ofatumumab over teriflunomide on annualised relapse rates. If both studies meet the primary endpoint, data will be combined to assess the key secondary disability-related endpoints.

Results: A pre-planned analysis of blinded data will be performed to: 1) re-assess sample size, increasing to a maximum of 1250 patients per study; 2) declare 'end of study' when each study is powered to 90% for primary and to $\geq 80\%$ for the combined analysis of key secondary endpoints ($\geq 90\%$ for 3-month confirmed disability worsening endpoint). The study duration is flexible, but capped at a maximum of 30 months in individual patients. Statistical analysis methods adequate for a study with flexible duration will be applied (e.g. Cox regression and negative binomial models with offset). The sample size and study duration adapt according to the activity of the study population to provide sufficient power.

Conclusion: An adaptive design with flexible study duration ensures minimum patient exposure to the double-dummy treatment that is required to address the scientific objectives.

Disclosure: This study was funded by Novartis Pharma AG, Basel, Switzerland. Detailed disclosure of each author will be included in the poster.

EP2155

Cancelled

EP2156

The role of serum netrin-1 in early multiple sclerosis

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Background and aims: Netrin (NTN)-1, a secreted laminin-related protein, is known to affect axonal guidance and neuronal cell migration, but also blood-brain barrier integrity and inflammation. Two preliminary studies reported altered serum NTN-1 levels in multiple sclerosis (MS), however associations with longitudinal clinical and MRI data have not been investigated. We aimed to assess serum NTN-1 in MS and controls with respect to disease, disease activity, and temporal dynamics.

Methods: We included 79 MS patients (clinically isolated syndrome CIS n=32, relapsing-remitting MS RRMS n=47; age mean \pm SD 33.9 \pm 8.8 years) and 30 non-inflammatory neurological disease controls (age mean \pm SD 37.1 \pm 10.2 years). Serum samples were drawn in all subjects, in patients during two gadolinium (Gd)-enhanced 3T MRI examinations (initial contrast-enhancing Gd+ n=47, non-enhancing Gd- n=32; reference Gd- n=70; median time-lag 1.4 (IQR 1.0-2.3) years). Clinical data of patients were recorded. Serum NTN-1 was assessed by ELISA (Cusabio, China).

Results: Serum NTN-1 levels were similar in CIS, RRMS and controls, and Gd+ and Gd- patients. Among patients with MRI-based signs of disease activity, those who experienced an apparent clinical relapse within 30 days prior to sampling (n=8) showed decreased serum NTN-1 levels compared to clinically non-active Gd+ patients (n=39; p=0.041). Serum NTN-1 levels showed no temporal dynamics in the MS patients and were unrelated to clinical data.

Conclusion: Our study cannot confirm any MS specific changes of serum NTN-1 levels and they appear not sensitive to MS disease activity as evidenced by contrast enhancing lesions on MRI. NTN-1 changes during clinical relapses may deserve further examination.

Disclosure: This study represents a sub-study supported by the Austrian Federal Ministry of Science, Research and Economics (core-study named 'BIG-WIG MS' (Bildgebung, Immunpathogenese, Gesundheitsfaktoren – Wien, Innsbruck, Graz – bei Multiple Sklerose); 'Neuroimaging, immunopathogenesis and salutogenic factors in MS – a collaborative effort of the universities of Vienna, Innsbruck and Graz')).

EP2157

Frequency of restless leg syndrome and related sonographic parameters of brain parynchyma in relapsing remitting multiple sclerosis

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Background and aims: Restless leg syndrome (RLS) has been reported in MS patients. which may reflects deep grey matter pathology, A recent tool in monitoring aspects of neurodegeneration and deep grey matter pathology is transcranial sonography (TCS).

Aims: To estimate the frequency of RLS among relapsing remitting MS (RRMS) patients and to investigate related sonographic changes in the echogenicity of deep grey matter (DGM) and ventricular diameters.

Methods: A case-control study, conducted on 125 Egyptian subjects: 54 RRMS patients according to revised MacDonald's criteria, 2010, (16 males, 38 females), with a mean age of 29.24 ± 8.23 and a mean EDSS of 2.34 ± 1.11 , and 71 age and sex matched healthy volunteers. All participants were subjected to clinical assessment and to the Cambridge-Hopkins RLS diagnostic questionnaire-short form-13. B-mode TCS of the brain parenchyma was done to evaluate ventricular diameter (marker of brain atrophy), and planimetric measurement of the DGM echogenicity (marker of neurodegeneration).

Results: MS patients showed significantly higher frequency of RLS (29.6%) compared with controls (7.04%) ($P=0.004$). MS/RLS+ subjects displayed significantly larger frontal horn diameter and larger substantia nigra (SN) surface area than control/RLS+ [$(0.45 \pm 0.11$ versus 0.32 ± 0.19 cm; $P=0.04$) & $(0.19 \pm 0.06$ versus 0.13 ± 0.05 cm²; $P=0.03$) respectively]. MS/RLS+ displayed significantly smaller surface area of the right red nucleus (RN) than MS/RLS- ($P=0.04$). None of the MS/RLS+ or control/RLS+ displayed the triad of RN hyperechogenicity, SN hypoechogenicity and interrupted raphe.

Conclusion: High frequency of RLS among RRMS patients may be related to a neurodegenerative process involving the SN.

Disclosure: Nothing to disclose

EP2158

The efficacy of patient education in preventing urinary tract infections in multiple sclerosis

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Background and aims: Urinary tract infections (UTI) are frequently observed in multiple sclerosis (MS) patients. Due to UTI, the treatment of MS becomes difficult and may be interrupted. Antibiotic use becomes necessary and a new MS attack may occur in this period. The aim of our study is to evaluate the efficacy of giving infection control training course to MS patients.

Methods: From January to November 2015, 72 registered MS patients of our clinic were recruited for this study. An infection control training course was conducted by the same specialized nurse of our hospital as a part of patient education programme for MS (23/05/2015). The pre-training period (Pre-TP) was between 01/January-22/May 2015 and the post-training period (Post-TP) was between 25 May and 01 November 2015. The demographic data, detailed medical history, neurological evaluation, symptoms for UTI and the haematologic and biochemical laboratory results were recorded from patient files. SPSS 18.0 was used for statistical analysis. $p < 0.05$ was accepted as the level of significance.

Results: Out of 72 MS patients, 46 (63.8%) were male, 26 (36.1%) were female. Mean age of the patients were 39.8 ± 10.0 (18-67). The number of MS patients who had UTI symptoms were 42/72 (58.3%) in the Pre-TP and 25/72 (34.7%) in the Post-TP ($p=0.004$).

Conclusion: Preventing infections will increase the quality of life of the patients and reduce the economic burden of the disease. Our study demonstrated that training MS patients to prevent infections effectively decreases the symptoms of UTI. A standardised and easily available infection control training programme should be developed for MS patients.

Disclosure: Nothing to disclose

EP2159

Effect of bilateral subthalamic deep brain stimulation on quality of life in Parkinson's disease

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Background and aims: Bilateral subthalamic deep brain stimulation (STN DBS) significantly improves motor symptoms in Parkinson's disease (PD). However, this motor improvement may not reflect the global therapeutic impact for the patient with regard to the social and emotional dimensions of the quality of life. The aim of this study was to assess the health related quality of life (HRQoL) in PD before and following STN DBS.

Methods: We evaluated 25 PD patients treated with STN DBS. HRQoL was assessed by both specific questionnaire of quality of life in PD -the Parkinson's Disease Questionnaire (PDQ39) and general quality of life-assessment questionnaires the Short Form 36 health survey questionnaire (SF36) and The World Health Organization Quality of Life Test-Bref (WHOQOL-BREF) 2 weeks before and 3,6,12 months after surgery.

Results: Before STN DBS the lowest rating of HRQoL was related to daily activities at the mean level of 68.8 points, followed by mobility with the average of 65.3 and 61.3 points noted for stigma of the disease per 100-point scale PDQ-39. Three months after STN DBS HRQoL improved in all domains assessed in PDQ-39, with the exception of social support and communication. The same improvements were observed in 6 months and 1 year follow-up. Using the SF-36 and WHOQol-Bref questionnaires before STN DBS, we noted a lower HRQoL within the physical compared to the mental dimension score. After STN DBS, the improvement was more pronounced in the physical than the mental score.

Conclusion: STN DBS significantly improved HRQoL as measured by PDQ-39, SF-36, WHOQol-Bref.

Disclosure: Nothing to disclose

MS and related disorders 4

EP2160

Disability progression in multiple sclerosis is biphasic with uniform trajectory after expanded disability status score of threeI. Uyanik¹, G. Tuncay¹, M. Kürtüncü², M. Eraksoy³¹Department of Neurology, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turkey, ²Istanbul, Turkey,³Istanbul, Turkey

Background and aims: Evidence suggests that multiple sclerosis (MS) has a two-stage progression rate before Expanded Disability Status Scale (EDSS) 6. In this study, we challenge the hypothesis that postulates a uniform progression rate of patients with MS between EDSS 3 and 6 despite disparate progression rates before EDSS 3.

Methods: We included patients with definite MS with a follow-up duration of at least one year. Demographic and clinical data including time to EDSS 3 and time to EDSS 6 were collected. We subgrouped the cohort according to their time to EDSS 3 and compared the rate of disability progression between EDSS 3 and 6 using Cox logistic regression.

Results: Of 876 (617 females, 259 males) patients, the ratios of MS subtypes were as follows: RRMS: 81.3%, SPMS: 9.8%, PPMS: 5.7%, and RPMS 3.2%. The most frequent symptoms at onset were sensory, optic neuritis, and sensory-motor in 19.3, 11.3, and 17.7% of patients respectively. After a mean follow-up duration of 8.8±7.1, 33.9% of patients reached EDSS 3 and 13.8% EDSS 6. Kaplan-Meier estimates of the mean time to EDSS 3 was 17.1±0.7 and the mean time to EDSS 6 was 28.8±1.8. We found nearly identical disability progression rates between EDSS 3 and 6 irrespective of time to EDSS 3 (Log rank test: p= 0.4) (Figure 1).

Figure 1: Kaplan-Meier estimate of the interval between EDSS 3 and 6 (p value was derived from log rank test).

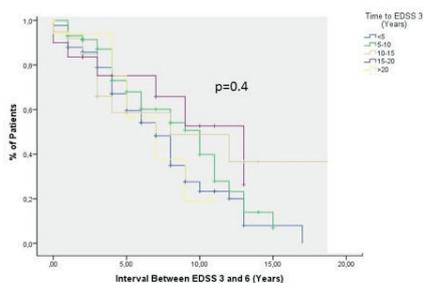


Figure 1

Conclusion: Our study confirms previous studies that suggest similar disability accumulation rates between EDSS 3 and 6 in patients with disparate progression rates between EDSS 0 and 3.

Disclosure: This study was sponsored by Neuroimmunological Society, Turkey.

EP2161

Cancelled

EP2162

Spanish registry of multiple sclerosis patients on glatiramer acetate 40 mg/ml treatment: Real-world results and baseline characteristics of initial patientsÓ. Fernández¹, X. Montalban²,A. Rodriguez-Antiguedad³, M.L. Martínez Ginés⁴,B. Casanova⁵, S. Moreno Garcia⁶, J. Martin Hernandez⁷,
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Background and aims: To describe the profiles of patients undergoing treatment with glatiramer acetate (GA) 40mg/ml in Spanish real-world clinical practice.

Methods: This is a prospective, observational, multicentre patient registry from 41 Spanish multiple sclerosis (MS) hospital units. Relapsing MS patients on GA 40 mg/ml treatment were recruited and will be followed for a maximum of 5 years. All patients' visits were performed as per daily clinical practice.

Results: During the first six months of the registry 970 patients were recruited (664 females, median age 44 years). Mean age at diagnosis of the disease was 36 years (range 28 to 42) and time from diagnosis to registry recruitment was 8 years. The majority of patients (n=757, 78.4%) had previously been treated with other immunomodulatory/immunosuppressive drugs before entering the study. Prior therapies included GA 20 mg/ml (60.4%), interferons (31.3%) and other drugs (8.4%).

Main reasons for switching from other therapeutic options were mainly induced by adverse events (19.2%) or lack of response (16.5%). Additional baseline characteristics included a mean EDSS of 2.0 the year prior to participation in the registry, and an annualized relapse rate of 0.4. The vast majority of patients (n=684, 70.5%) showed no relapses during the 12 month period before entering the registry.

Conclusion: The baseline data from the 970 patients included in the Spanish GA 40 mg/ml registry indicate that the population is characterized by low disease activity (low relapse rate, lesion load, and mild disability scores).

Disclosure: This research has been supported by TEVA pharmaceuticals

EP2163

Cerebrospinal fluid and serum levels of interleukin-8 in patients with multiple sclerosis and its correlation with other markers

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Background and aims: The result of inflammatory and neurodegenerative processes in Multiple Sclerosis (MS) is axon and myelin breakdown. The paraclinical examination methods (MRI and an examination of cerebrospinal fluid (CSF)) are an important part of the diagnostic process. An increasing number of studies deal with CSF and serum levels of biomarkers and their role in MS. We hypothesized that the level of interleukin-8 (IL-8) could be different in MS patients than in controls. In the second step we hypothesized that the blood-brain barrier is damaged in the early stages of MS.

Methods: CSF and serum levels of IL-8 were assessed in 102 patients with newly diagnosed MS meeting McDonald's revised diagnostic criteria and in 102 subjects as a control group. We then correlated these results with Q-alb, oligoclonal bands and light chains.

Results: Levels of IL-8 in CSF were significantly higher in MS patients than in controls (Mann-Whitney U test, $p < 0.0001$). Spearman's correlation analysis proved a significant correlation between levels of IL-8 and Q-alb, IL-8 and oligoclonal bands, IL-8 and light chain lambda.

Conclusion: Based on our results, we hypothesized that IL-8 could partially come from the periphery, and that IL-8 could penetrate through the damaged BBB. This may be the reason that IL-8 is increased in CSF and decreased in serum in patients with MS. On the other hand, there were general opinions that the IL-8 is produced de novo in the CNS. The results also confirm the presence of inflammatory processes in the early stages of MS.

Disclosure: This work was supported by the Institutional support of the Research Organisation - Ministry of Health, Czech Republic, RVO - FNOL 2016

EP2164

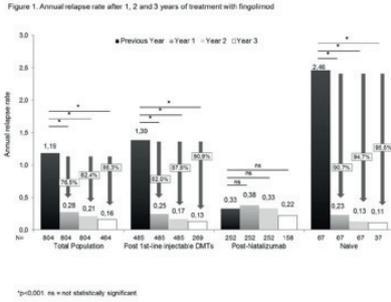
Effectiveness of fingolimod in patients with relapsing-remitting multiple sclerosis in daily clinical practice in Spain: Results from a multivariate pool analysis called Fingoview

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Background and aims: Once-daily fingolimod (Gilenya[®], Novartis Pharma AG) is a sphingosine 1-phosphate receptor modulator approved for relapsing MS treatment. Continuous collection and analysis of real world effectiveness and safety data is key to making accurate treatment decisions. The objective is to describe basal characteristics and effectiveness of fingolimod in patients with relapsing-remitting multiple sclerosis (RRMS) followed for ≥ 12 months in routine clinical practice in Spain.

Methods: Fingoview is a multivariate pool analysis of two observational, retrospective chart review, multicenter studies MS SECOND LINE GATE and MS NEXT, conducted in specialized MS centers in Spain, between November 2014 and December 2015. Pool analysis was prospectively planned. Both studies included patients of both sexes, ≥ 18 years, diagnosed with RRMS, treated with fingolimod according SmPC and followed up for ≥ 12 months after treatment initiation.

Results: Fingoview included 988 patients (70 naïve, 252 post-natalizumab, 666 post first-line injectable DMTs), 68.9% female, mean(SD) age: 40.44(9.1) years (Table 1). After 1, 2, 3 years of treatment mean annual relapse rate decreased by 76.5%(mean: 1.19 to 0.28), 82.4%(0.21) and 86.3%(0.16) compared to the year prior to fingolimod (all $p < 0.0001$) (Figure 1). At 12 months, 89.6% of patients had stable or improved EDSS which was maintained in 84.4% of patients at 24 months (Figure 2). New/enlarged T2 lesions, gadolinium-enhancing lesions on T1 or radiologically disease free will be discussed.

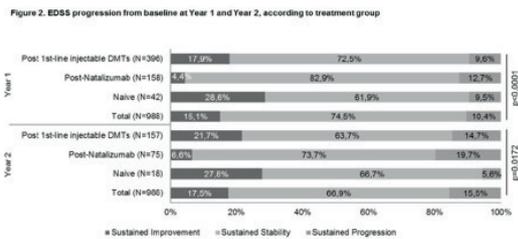


Annual relapse rate after 1, 2 and 3 years of treatment with fingolimod

		Post 1 st -line injectable DMTs (N=666)	Post-NTZ (N=252)	Naive (N=70)	Total (N=988)	p-value
Age, years	Mean (SD)	40.3 (8.9)	41.4 (8.8)	38.6 (9.5)	40.4 (9.1)	0.0449
	Range	(20 - 69)	(20 - 63)	(18 - 64)	(18-69)	
Sex, females	N (%)	474 (71.2%)	162 (64.3%)	45 (64.3%)	681 (68.9%)	0.0905
Time from MS diagnosis to start of fingolimod, in years	Mean (SD)	8.2 (5.8)	10.4 (5.5)	4.4 (6.4)	8.5 (5.9)	<0.0001
Time of treatment with fingolimod, in years	Mean (SD)	2.2 (0.8)	2.2 (0.9)	2.1 (0.9)	2.2 (0.8)	NA
ARR previous year	Mean (SD)	1.4 (0.9)	0.3 (0.8)	2.5 (1.8)	1.3 (1.1)	<0.0001
Number of relapses in the last 2 years	Mean (SD)	1.9 (1.2)	0.4 (0.9)	2.0 (1.03)	1.6 (1.3)	<0.0001
EDSS at study start	Mean (SD)	2.9 (1.5)	3.5 (1.8)	2.6 (1.8)	3.0 (1.6)	<0.0001
	Median (IQR)	2.5 (2.0-4.0)	3.5 (2.0-4.5)	2.5 (1.5-3.5)	3.0 (2.0-4.0)	
Number of T1 Gd-enhancing lesions	N	405	57	40	502	<0.0001
	Mean (SD)	1.37 (2.8)	0.25 (1.2)	1.68 (2.6)	1.26 (2.7)	
Number of T2 lesions**						
< 9 lesions	No. patients (%)	25 (6.3%)	4 (7.4%)	7 (17.1%)	36 (7.3%)	0.0539
9 - 20 lesions	No. patients (%)	160 (40.2%)	28 (51.9%)	14 (34.1%)	202 (41.0%)	0.1711
> 20 lesions	No. patients (%)	213 (53.5%)	22 (40.7%)	20 (48.8%)	255 (51.7%)	0.1956

SD: Standard deviation. IQR: Interquartile range. NA = Not available
 *Patients who had a baseline MRI during washout period were excluded (61 in the final sample)
 **Calculations performed without Not Available category

Baseline characteristics



EDSS progression from baseline at Year 1 and Year 2, according to treatment group

Conclusion: After switching to fingolimod, RRMS had significantly suppressed clinical disease activity and most of the patients have a stable EDSS after one year of treatment.

Disclosure: Study Supported by: Novartis Farmacéutica S.A.

EP2165

Baseline cognitive impairment predicts one year disease progression in MS

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Background and aims: Cognitive impairment commonly affects Multiple Sclerosis (MS) patients and may have a dramatic impact on their quality of life, performance at work and social life. We aimed to assess the ability of specific computerized real-time cognitive tests to predict disability progression at 1 year after initiating immunomodulatory treatment for MS in comparison with the predictive value of the Expanded Disability Status Scale (EDSS).

Methods: Fifty three Relapsing-Remitting (RR) MS patients (F=42, mean age 36.02±9.25, mean EDSS 2.18±1.27) who started immunomodulatory treatment with glatiramer acetate or interferon beta preparations underwent cognitive evaluation using a computerized real-time battery of basic neuropsychological tests (“CogScan”; Anima Scan LTD), which includes: Finger Tapping Test (FTT), Simple Reaction Time (SRT), Choice Reaction Time (CRT), Immediate and Delayed Memory for Pictures, Words and Faces and Digit Running Test (DRT). EDSS scores were recorded every 3 months. Univariate logistic regression analysis was conducted for each predictor and the most robust predictor was analyzed by Receiver Operating Characteristic (ROC).

Results: At 1 year, 9 patients (17%) had 3-months sustained disability progression. Baseline EDSS could not predict disability progression, while assessment of simple cognitive functions yielded four statistically significant predictors: Standard deviation (SD) in both FTT and DRT, accuracy and latency in the DRT. The DRT-I SD showed the best predictive value for disability progression.

Conclusion: Baseline cognitive assessment, especially slow and highly variable performance on the DRT, but not baseline EDSS, can predict the progression of neurological disability after one year of immunomodulatory treatment in RRMS.

Disclosure: This study has been partially supported by research grants from Teva pharmaceuticals, Merck-Serono and Medison, Israel.

EP2166

Oxidative stress in multiple sclerosis: Effect of dietary supplementation with coenzyme Q10

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Background and aims: Oxidative stress plays an important role in multiple sclerosis (MS). We evaluated the effect of coenzyme Q10 (CoQ10), a compound with marked antioxidant effects, on MS-related laboratory and clinical outcomes.

Methods: We analysed serum and clinical data from 60 relapsing-remitting MS patients (age 42.3 ± 8.9 years; female 70%). Data were collected after 3 months of CoQ10 dietary supplementation (Skatto[®], ChiesiFarmaceuticiSpA, 200mg/day) and during additional 3 months either before or after CoQ10 supplementation (no-CoQ10 status). Treatment with subcutaneous high-dose interferon beta-1a was maintained during the study period (Rebif[®], Merck Serono SpA, 44microg/week). Laboratory outcomes included markers of free radical scavenging activity, oxidative damage and neuroinflammation. Patient-reported outcomes included questionnaires for cognition, fatigue, depression, pain and headache. Clinical outcomes included occurrence of relapses and EDSS variations.

Results: Regression models adjusted for age, gender, disease duration, duration of interferon beta-1a treatment and EDSS were used. Patients receiving CoQ10 supplements had a 0.6 mg increase in uric acid (Coeff=0.556; 95%CI=0.179-0.933; p=0.004), compared with no-CoQ10 status. After receiving CoQ10 supplements, patients presented with improved cognitive scores on the MS neuropsychological questionnaire (Coeff=6.472; 95%CI=1.197-11.748; p=0.016), and with reduced pain on the visual analogue scale (Coeff=-1.899; 95%CI=-3.608--0.189; p=0.029).

Conclusion: Restoring an appropriate oxidative balance with CoQ10 dietary supplementation in combination with disease modifying treatment may be responsible for an improvement in patient-related outcomes such as cognition and pain. In the long-term, it is possible to hypothesize that a reduction in oxidative stress might exert positive effects on the disease course of MS. Future studies on larger populations and with longer follow-up are required to confirm present findings.

Disclosure: The present research received support by Merck Italy.

EP2167

A post-marketing observational monocentric study

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Background and aims: Registrative studies showed the effects of Dimethyl Fumarate (DMF), however real life studies are needed to confirm these results.

Methods: Currently, 444 RRMS patients are treated with DMF at San Raffaele Hospital. 255 pts received DMF for at least 12 months. 70.2% female, mean age 37.2; mean disease duration 10.2; mean EDSS 1.87. 16.9% of pts were naïve, 49.7% switched to DMF from injective disease modifying therapies (DMT) for intolerance, 24.7% for inefficacy, 7.4% for convenience (JC+ in Natalizumab or from Cyclophosphamide). All pts had a brain MRI at DMF initiation and a neurological examination every 3 months. The 74.9% had a MRI follow up at 6 months, the 53.6% at 12 months.

Results: At the last FU: 86.7% were relapse free. Compared to the year before treatment mean ARR was reduced from 0.35 to 0.1 (Wilcoxon; p<0.001); ARR reduction was significant (p<0.001) also in all subgroups: naïve, switchers for intolerance or inefficacy. The percentage of patients with active MRI was reduced from 34.5% to 14.8% (p<0.001). The analysis of ARR reduction in switchers from DMT for inefficacy could be biased by higher ARR before DMF; in fact, in these pts, ARR during DMF treatment was 0.175 whereas it was 0.04 in switchers for intolerance (Wilcoxon; p=0.012). DMF was well tolerated, 5% of patients discontinued for GI symptoms, 0.3% for flushing and 2.7% for lymphopenia.

Conclusion: Our data confirm the efficacy and safety of DMF as first line treatment for naïve pts or switchers from DMT for intolerance/mild inefficacy.

Disclosure: I received speaking and travel honoraria from: Biogen, TEVA, Merck, Genzyme

EP2168

Alemtuzumab post authorization safety study (PASS) study design: Evaluating the long-term safety profile of alemtuzumab in patients with RRMS

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Background and aims: Alemtuzumab is a humanised anti-CD52 monoclonal antibody approved for the treatment of relapsing-remitting MS (RRMS) in >60 countries. Alemtuzumab significantly improved clinical and MRI outcomes versus subcutaneous interferon beta-1a (CARE-MS I [NCT00530348]; CARE-MS II [NCT00548405]) over 2 years in patients with RRMS. Efficacy was durable through 6 years in the absence of continuous treatment (NCT00930553). Here we describe the design of the PASS study, which will further evaluate the necessary duration and appropriate safety monitoring conditions, including incidence of adverse events of special interest (AESI), after alemtuzumab treatment in RRMS patients under conditions of real use.

Methods: PASS is an international, prospective, multicentre, observational study. Duration per patient will be 10 years under the protocol amendment approved in US, currently under review by EMA. Inclusion criteria: patients with RRMS, having initiated alemtuzumab for the first time ≤8 weeks before enrolment. Target enrolment: 5000 worldwide (67% in Europe). Primary endpoint: incidence of AESI, defined as serious infection, pneumonitis, malignancy, and autoimmune-mediated conditions. Secondary endpoints: descriptive statistics on the natural history of incident AESI; relative risk of AESI in alemtuzumab-treated versus non-alemtuzumab-treated MS patients (external comparison cohort); potential associations between risk factors and incidence of AESI; incidence of AEs and SAEs; demographic and clinical characteristics of patients, and description of alemtuzumab utilization patterns.

Results: Enrolment is currently ongoing. Results will be reported following study completion.

Conclusion: The PASS study will evaluate the long-term safety profile of alemtuzumab treatment in patients with RRMS under real conditions of use.

Disclosure: Sanofi.

EP2169

Cancelled

EP2170

Smoking prior to multiple sclerosis diagnosis is associated with worse prognosis

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Background and aims: Smoking is a modifiable risk factor of multiple sclerosis (MS). There are controversial results about its influence on long-term disability progression. We investigate here the correlation between the number of smoking years and of packets-year accumulated at diagnosis with disability later on.

Methods: MS patients who accepted to complete a self-administered questionnaire (98%) about their exposure to tobacco were randomly selected. We also collected clinical and demographic variables from our database.

Results: 134 MS patients (69% women, 31% men). Mean age 40.32 (18-65) years. Mean duration of disease 10.45 (10-42) years. 35% smokers, 38% never smokers and 27% former smokers. A very significant positive correlation was found between the number of smoking years and packets-year accumulated at diagnosis and disability at the moment of the study (p<0.01) or disability during the first nine years after diagnosis (table 1). A statistically significant difference in time to reach EDSS 3.0 was found between smokers and non smokers before diagnosis of the disease (p<0.05). (Figure 1).

		EDSS YEARS AFTER DIAGNOSIS									
		EDSS AT CURRENT MOMENT	1	2	3	4	5	6	7	8	9
AT DIAGNOSIS	NUMBER OF SMOKING YEARS	R = 0,25**	R = 0,37**	R = 0,28**	R = 0,31**	R = 0,32**	R = 0,30**	R = 0,28*	R = 0,35**		R = 0,37*
	PACKETS-YEAR ACCUMULATED	R = 0,23**	R = 0,34**	R = 0,27**	R = 0,30**	R = 0,31**	R = 0,27*	R = 0,26*	R = 0,34*	R = 0,37*	R = 0,38*

* p<0,05; ** p<0,01.

Table 1. The table shows the correlation between the number of smoking years and packets-year accumulated at diagnosis and the disability as measured by EDSS in the first nine years after diagnosis and at the moment of the study. We found a significant positive correlation in each moment analyzed.

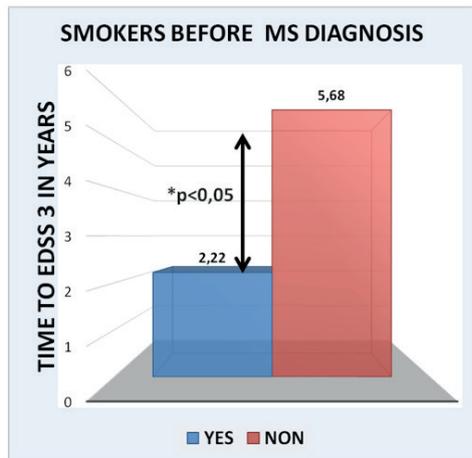


Figure 1. This figure shows that smoker patients before the MS diagnosis reach EDSS 3.0 before non smoker patients. We found a statistically significant difference ($p < 0,05$) between groups.

Conclusion: MS patients who had smoked before the diagnosis of the disease had a more severe disease course and a faster disability progression rate (Figure 2).

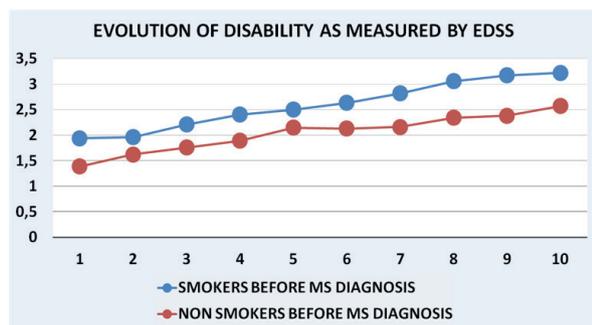


Figure 2. The figure shows the evolution of the disability as measured by EDSS in smoker and non smoker patients before MS diagnosis. A more severe disease course and a faster disability progression rate was found in patients who had been smokers before MS diagnosis. MS= multiple sclerosis.

Disclosure: Nothing to disclose

EP2171

Lymphocyte recovery in real life clinical practice after discontinuation of fingolimod in patients with multiple sclerosis

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Background and aims: Fingolimod induces a fast reduction of lymphocyte counts in the blood, however, less is known about the recovery of immune cells after treatment discontinuation in real life clinical practice.

Methods: We examined leukocyte, lymphocyte and neutrophil counts of 35 patients with multiple sclerosis, 90 (mean 80.6), 180 (mean 195.1) and 365 (mean 358.3) days after stopping fingolimod. Blood tests were available in 33 patients for the first and in 30 patients for the second and third time point. Leukopenia was defined as ≤ 3500 , lymphopenia as ≤ 900 , neutropenia as ≤ 1300 cells per microliter. We included age, fingolimod treatment duration, mean interruption before therapy switch, lymphocyte count at therapy switch and previous immunomodulatory regimens into our analysis to determine potential influencing factors of immune cell recovery.

Results: All patients showed a drop of lymphocyte count under fingolimod with no relevant leukopenia or neutropenia. Three months after treatment discontinuation 6 patients, while six and twelve months later still 5 patients showed decreased lymphocyte levels. Four out of these 5 patients received rituximab as a follow-up treatment. 44% (4 out of 9) patients that switched to rituximab showed a prolonged lymphocyte recovery. Lymphopenia at start with rituximab and pretreatment with mitoxantrone seemed to be contributing factors to a prolonged lymphopenia.

Conclusion: We observed lymphopenia in 16.7% of patients 1 year after discontinuation of fingolimod. Successive treatment with rituximab, low lymphocyte count at therapy switch, and pretreatment with mitoxantrone might contribute to a prolonged immune cell recovery. This should be considered when changing treatment regimens.

Disclosure: The institution (University Hospital Basel) received in the last 3 years and used exclusively for research support: steering committee, consulting and speaker fees from Actelion, Addex, Bayer HealthCare, Biogen, Biotica, Genzyme, Lilly, Merck, Mitsubishi, Novartis, Ono, Pfizer, Receptos, Sanofi-Aventis, Santhera, Siemens, Teva, UCB and Xenoport; support of educational activities from Bayer HealthCare, Biogen, CSL Behring, Genzyme, Merck, Novartis, Sanofi-Aventis and Teva; royalties from Neurostatus Systems GmbH; grants from Bayer HealthCare, Biogen, the European Union, Merck, Novartis, Roche, the Swiss Multiple Sclerosis Society and the Swiss National Research Foundation.

EP2172

Pregnancy outcomes following ocrelizumab treatment in patients with multiple sclerosis and other autoimmune diseases

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Background and aims: Ocrelizumab has been studied as a treatment in multiple sclerosis (MS), rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). This report reviews pregnancy outcomes in women treated with ocrelizumab.

Methods: This analysis included women who received ocrelizumab (20–2000 mg) in clinical trials of MS, RA or SLE. Two methods of contraception were required during the trials and for 1 year/48 weeks after the last ocrelizumab infusion or until B cells repleted, whichever was longer. An embryo/foetus was considered exposed to ocrelizumab if the last infusion occurred within 3 months of conception, during pregnancy or if the date was unknown.

Results: This analysis included 46 women (15 MS, 10 SLE, 21 RA) who reported 48 pregnancies (15 MS, 11 SLE, 22 RA) between 2008 and 14 September 2015. Among patients with MS, seven pregnancies with foetal ocrelizumab exposure ended in one healthy term baby and four elective terminations; two pregnancies were ongoing at the time of analysis. Seven pregnancies without foetal ocrelizumab exposure ended in two healthy term babies; one infant born at 34 weeks' gestation with nasopharyngeal neoplasm, jaundice, respiratory disease and low birth weight; two elective abortions; and two ongoing pregnancies. One pregnancy with unknown foetal ocrelizumab exposure ended in elective termination. Additional pregnancy outcomes in patients with SLE and RA will be reported.

Conclusion: Considering the prevalence of MS among women of reproductive age, pregnancy outcomes in treatment-exposed patients are important to understand. Pregnancy outcomes in ongoing ocrelizumab studies will continue to be assessed and reported.

Disclosure: Sponsored by F. Hoffmann-La Roche Ltd.

Muscle and neuromuscular junction disease 2

EP2173

Low serum vitamin D levels in patients with myasthenia gravis

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Background and aims: Myasthenia gravis (MG) is a chronic autoimmune neuromuscular disease. Vitamin D has important roles both in the autoimmune response and in skeletal muscles. We investigated the levels of 1, 25-dihydroxy vitamin D [1, 25(OH)2D] and 25-hydroxy vitamin D [25(OH)D] in patients with MG and healthy subjects.

Methods: Plasma levels of 1, 25(OH)2D and 25(OH)D were analyzed in 25 patients with MG and in 40 healthy age- and sex-matched healthy controls. MG patients were classified by disease stage (ocular or generalized) and treatment status whether or not to taking immunosuppressive agents. In addition, the MG composite (MGC) scale was assessed to evaluate the disease severity.

Results: MG patients without pre-existing vitamin D3 supplementation had lower plasma 25(OH)D levels (mean, 18.8±8.4 ng/mL) than healthy controls (26.3±6.1 ng/mL) ($p < 0.05$). 1, 25(OH)2D levels showed slightly high in MG patients (46.4±21.9 ng/mL) than healthy controls (42.1±7.0 ng/mL), but had no significant difference between two groups. Vitamin D levels of 1,25(OH)2D and 25(OH)D did not significantly differ between ocular and generalized MG. In addition, levels of vitamin D did not significantly differ between MG patients under immunosuppressive therapy and taking anti-cholinesterase only. No correlation was observed between MGC scale score and 25(OH)D levels.

Conclusion: Plasma 25(OH)D levels significantly lower in patients with MG compared with healthy controls. We recommend monitoring of vitamin D status in patients with MG to avoid direct negative effects on the muscles or autoimmune response.

Disclosure: Nothing to disclose

EP2174

Cancelled

EP2175

Thymoma associated myasthenia gravis in Slovak Republic - a cohort of 129 patients (1978 - 2016)

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Background and aims: For immunopathogenesis of thymoma associated myasthenia gravis (TAMG) is typical combined presence of intrathymic (thymus, thymoma) and extrathymic autoimmune mechanisms.

Objective: We performed retrospective longitudinal study of 129 patients with TAMG registered at Slovak Centre for Neuromuscular Diseases in the years 1978-2016. The aim of the study was to analyze epidemiological and clinical data, laboratory findings and prognostic factors in TAMG.

Methods: We analyzed data and findings in medical records of TAMG patients including age at onset, sex, autoantibodies against acetylcholine receptors (AChRs), type of clinical symptomatology. We evaluated used therapies, clinical status at the last examination and prognosis of TAMG.

Results: Out of 2168 MG patients we found TAMG in 129 patients (6.0%), 49 men and 80 women. The mean age at disease onset was 51.7 years. We found positive titer of anti AChR antibodies in sera of all TAMG patients, except one. In 78 patients (63.4%) remission or significant improvement by immunotherapy and surgical treatment was achieved. MG was no primary cause of death for the last 20 years. 94 patients had benign and 35 malignant thymoma. Six patients with malignant thymoma died on thymoma dissemination, four out of them had MG in remission.

Conclusion: Both, MG severity and biological characteristics of thymoma, determine TAMG prognosis. Early diagnosis and optimal treatment of TAMG are crucial for favorable prognosis. Key words: myasthenia gravis, thymoma, epidemiology, diagnosis, treatment, prognosis

Disclosure: Nothing to disclose

EP2176

Electrophysiological investigation of autonomic involvement in patients with myasthenia gravis

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Background and aims: Myasthenia gravis (MG) is a autoimmune disorder of the neuromuscular transmission and has not a known association with autonomic dysfunction. There are however rare reports of MG coexisting with autonomic failure. We therefore conducted this study to evaluate autonomic functions electrophysiologically in patients with MG and find out subclinical autonomic disturbance.

Methods: This study comprised 29 autoimmune MG patients who were followed at Istanbul University Cerrahpasa Medical Faculty Neurology Department. Baseline characteristics for each patient were recorded. Sympathetic Skin Response (SSR) and R-R Interval Variability (RRIV) was carried out. The tests were performed two times for patients who were under acetylcholinesterase inhibitors: at the end of the longest period of time may be drug-free and an hour after taking the drug. The results of patients were compared with age and gender matched 30 normal subjects.

Results: There was no significant difference between the patient and the control groups' SSR results. The RRIV increased in both groups during hyperventilation as expected, but the rise was better in the control group ($p=0.006$). Valsalva ratio was lower in the patient group ($p=0.039$). The SSR results were compared prior to drug intake and afterwards; amplitudes of SSR were lower thereafter drug intake ($p=0.030$). There was no significant difference in SSR values according to the daily total dose of acetylcholinesterase inhibitors; but as much as time goes by after drug administration prolonged SSR latencies were obtained ($p=0.043$).

Conclusion: This study suggests that MG patients have a subclinical parasympathetic abnormality and piridostigmine has a peripheral sympathetic cholinergic noncumulative effect on these autonomic tests.

Disclosure: Our study was granted by Istanbul University | Scientific Research Projects Unit.

EP2177

Distinct clinical and genetic findings in Iranian patients with glycogen storage disease type 3

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Background and aims: glycogen storage disease type 3 (GSD-III) is a rare inherited metabolic disorder caused by glycogen debranching enzyme deficiency in liver, skeletal and cardiac muscles. Different pathogenic mutations of the AGL gene have been reported so far. Here, we report distinct clinical and genetic data of Iranian GSD-III patients.

Methods: clinical and laboratory data of 5 patients with GSD-III were recorded. Genetic analysis was performed to identify the causative mutations.

Results: Three of patients had typical liver involvement in childhood and one was diagnosed 2 years after liver transplantation for cirrhosis of unknown etiology. One of our patients presented with preferential involvement of skeletal muscles with an unusual pattern. All patients had homozygous mutation of AGL gene including 5 novel mutations: c.378T>A, c.1183C>T, c.3295T>C, c.3777G>A, c.2002-2A>G.

Conclusion: This is the first comprehensive report of patients with GSD-III in Iran. We have reported 2 uncommon clinical presentations and 5 novel mutations.

Disclosure: Nothing to disclose

EP2178

Detection of two novel DMD variants in a family with suspected hereditary muscular dystrophy

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Background and aims: A pair of twins (female and male) presented with muscle hypotonia of unknown genesis in the neonatal period. The father of the twins was diagnosed with Becker muscular dystrophy with first symptoms appearing at age 20. The purpose of the request was to perform molecular genetic analysis to test for hereditary muscular dystrophy.

Methods: To address this issue, Next Generation Sequencing (NGS)-gene panel analysis for muscular dystrophies was performed, followed by targeted carrier testing and segregation analysis.

Results: NGS-gene panel analysis of the twins DNA revealed a likely pathogenic variant and a variant of unknown significance (VUS) in the DMD gene. The detected variants had no known allele frequency and both variants have not yet been described in association with dystrophinopathies. The male twin was a hemizygote for the missense VUS c.5601A>C; p.Gln1867His, which results in the substitution of an amino acid at a highly conserved position in vertebrates. In the female twin the analysis revealed the variant identified in the brother, c.5601A>C; p.Gln1867His, and in addition the likely pathogenic frameshift variant c.79dupG; p.Ala27Glyfs*5, both in a heterozygous state. Subsequent testing of the parents showed that the symptomatic father was a hemizygote for the frameshift variant, the healthy mother was a heterozygous carrier of the missense VUS.

Conclusion: Based on the molecular genetic testing results of all family members we assume that both previously unreported DMD variants c.5601A>C; p.Gln1867His and c.79dupG; p.Ala27Glyfs*5 are most likely causative for the muscular dystrophy in the family.

Disclosure: Nothing to disclose

EP2179

Cancelled

EP2180

MicroRNAs and imaging phenotypes of trasportinopathy (limb-girdle muscular dystrophy type 1F)

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Background and aims: We report muscle histopathological, ultrastructural and radiological features of a large Italian-Spanish family with autosomal dominant LGMD, previously mapped to 7q32.2-32.2 (LGMD1F). Transportin-3 (TPNO3), which was found by NGS to be the causative gene in LGMD1F, is suggested to mediate the nuclear import-export. The non-stop mutation identified in this family encodes for a longer protein which is expected to be unable to move to the nucleus. Clinical phenotype penetrance in this family correlates at 92% with mutation presence.

Methods: We collected serum microRNAs, clinical history, muscle biopsies histopathology of one LGMD1F kindship. Biopsy of two affected patients mother and daughter was studied (in the daughter two consecutive biopsies at 9 and 28 years and in the mother at 48 years). MicroRNA especially miR-206 was several fold up-regulated in the daughter that hard relates at 92% with mutation presence.

Results: The daughter has a severe clinical course and the fiber atrophy was more prominent in the second biopsy at 28 years. The mother has a relatively compromised histopathology and many small muscle fibers, and autophagic changes by acid-phosphates stain. Immunofluorescence against desmin, myotilin, p62 and LC3 showed accumulation of myofibrils, ubiquitin binding proteins aggregates and autophagosomes. Ultrastructural analysis revealed myofibrillar disarray, vacuolar changes, granular material and dense subsarcolemmal bodies deriving from cytoskeleton-myofibrillar proteins. We hypothesize that the pathogenetic mechanism in LGMD1F might lead to disarrangement of desmin-associated cytoskeletal network.

Conclusion: Both microRNAs and muscle imaging are powerful tools in follow up of LGMD-1F patients

Disclosure: Nothing to disclose

EP2181

A novel mutation in collagen XII causing Ullrich-like muscular dystrophy

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Background and aims: Mutations in three known collagen type VI genes (COL6A1, COL6A2, COL6A3) are responsible for a spectrum of myopathies, that range from the mild Bethlem myopathy to the more severe congenital Ullrich muscular dystrophy. Not all those patients have mutations in collagen VI. Recently, mutations in COL12A1 have been reported to cause myopathies similar to those caused by mutations in collagen VI. To date, nine patients with collagen XII mutations have been reported: six patients from 3 families with Bethlem-like myopathies and 3 patients with a more severe congenital form. We report a case of a patient with a novel mutation in collagen XII causing a phenotype resembling Ullrich muscular dystrophy.

Methods: We describe a one-year-old portuguese boy, who presented with profound axial hypotonia from the first month of life. The boy has a marked kyphoskoliosis, pectus excavatum, retrognathia, ogival palate and cryptorchidism. His mother had had a previous gestation, with oligoamnios and spontaneous abortion at 20 weeks.

Results: We identified two rare variants in COL12A1 gene. One of them is a truncating mutation (W2332X) and the other one is a missense variant (C2739R) which is predicted as deleterious by CONDEL and GERP values.

Conclusion: We report a mutation in the collagen XII gene causing a Ullrich muscular dystrophy phenotype. This expands the spectrum of collagen XII mutations, that can lead to a wide spectrum of phenotypes ranging from severe Ullrich congenital muscular dystrophy-like forms to intermediate forms to milder Bethlem-like myopathies, similar to what happens with collagen VI mutations.

Disclosure: Nothing to disclose

EP2182

Serum vitamin D value is reduced in patients with myotonic dystrophy type 1

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Background and aims: Recently, vitamin D deficiency in patients myotonic dystrophy type 1 (DM1) was reported. Vitamin D deficiency is responsible of a secondary hyperparathyroidism or adverse effect of muscle strength in proximal muscles. The aim of this study was to investigate vitamin D deficiency state in DM1.

Methods: Forty-five genetically diagnosed DM1 patients with stable condition over three months (17 females and 28 males) were participated. The mean value of age was 47 years, and the number of CTG repeat (CTGn) was 1095. Serum level of 25-hydroxyvitamin D (OHD), 1,25dihydroxyvitamin D (OH2D), intact parathormone, Ca, and P were examined. Bone density was measured by dual-energy X-ray absorptiometry method. Body mass index (BMI) was calculated. Subjects were divided into two group according to motor disability, and data in each group were compared.

Results: OHD value was 10.8 ± 5.7 ng/ml (mean \pm SD). Markedly reduced OHD less than 10 ng/ml was observed 58% of patients. Whereas, OH2D was 46.6 ± 17.2 pg/ml and only 7% of patients showed low value. High value of parathormone was recognized in 9%. Hypocalcemia was in 4%. There was positive significant correlation between OHD and BMI, and negative correlation between OHD and parathormone or age. There was no significant correlation between OHD and CTGn. No evaluated items except for BMI indicated significant difference between the ambulatory group and the wheelchair or bedridden group.

Conclusion: Markedly reduced vitamin D level was common in patients DM1. However, it is still obscure what kind of symptoms vitamin D deficiency particularly affects in DM1.

Disclosure: Practical Research Project for Rare / Intractable Diseases from Japan Agency for Medical Research and Development(16ek0109172h003)

EP2183

Pseudo-dominant inheritance of a novel homozygous HACD1 mutation associated with congenital myopathy: The first Caucasian family

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Background and aims: Congenital myopathies are a clinical and genetic heterogeneous group of early onset muscle diseases. Mutations in HACD1 gene cause congenital centronuclear myopathy in dogs and have been recently described in one consanguineous Bedouin family with congenital myopathy that improved with age. We report herein the second family with congenital myopathy due to HACD1 mutations.

Methods: Clinical data were collected from the family members. Skeletal muscle biopsies were performed in two patients. The HACD1 mutation was identified by next-generation sequencing.

Results: The proband is a 28-year-old woman with facial and limb-girdle muscle weakness, that was born from consanguineous Caucasian parents. At birth, she presented with severe hypotonia that gradually improved. Muscle biopsy at 10 years of age revealed myopathic features with increased variation in myofiber size, type-1 fibers predominance, and slightly increased internal nuclei. The younger sister had similar clinical and histopathological findings. The mother and maternal grandmother had a slowly progressive proximal muscle weakness since childhood but, after neurological evaluation, surprisingly, also the father showed the same clinical picture. A novel homozygous variant in HACD1 gene (p.G213A) was detected in all the affected members.

Conclusion: To our knowledge, this is the second report on human mutations in HACD1. Our data highlight the implication of HACD1 in human pathology. Moreover, the long term follow-up of the affected individuals, revealed a mild and slowly progressive course, even at advanced age, which constitutes an important finding for patients' counseling.

Disclosure: Nothing to disclose

EP2184

Subclinical myocardial involvement in dysferlin deficient patients

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Background and aims: Different phenotypes have been recognized caused by mutations in dysferlin gene (DYSF): limb-girdle muscular dystrophy 2B, Miyoshi myopathy, and distal myopathy of anterior tibialis. Dysferlin is a large protein involved on plasma membrane repair. Recent evidence suggests that dysferlin deficiency could affect cardiac muscle, leading to cardiomyopathy.

We aim to identify a subclinical myocardial involvement in patients with molecular confirmation of dysferlin deficiency.

Methods: We conducted an observational prospective study of patients with molecular diagnosis of dysferlinopathy. Ten patients were enrolled and were subject to cardiac magnetic resonance (CMR) on a standard 1.5 Tesla clinical scanner with cine imaging for left ventricular volume (LVV) and ejection fraction (EF) calculation, and late post-gadolinium enhancement imaging (LGE) to assess for myocardial fibrosis.

Results: There was a slight predominance of male gender (60%). Mean actual age and age at diagnosis was 44.80 and 26.60 years, respectively. CMR revealed an average LVV of 147,5mL and average EF of 63%. One patient presented with severe dilated cardiomyopathy (LVV 329 mL and EF 29%). LGE imaging showed focal intramyocardial fibrosis in 3 patients (30%), two of these were asymptomatic. None of the clinical and laboratory parameters (functional status, CPK levels and molecular study) correlated with LGE.

Conclusion: Evidence of subclinical cardiac involvement in dysferlinopathies is increasing, although its real impact remains to be assessed. Phenotypic correlations were not able to yield any clinical predictor of LGE presence. Further studies are needed to evaluate the prognostic significance of subclinical findings detected by CMR.

Disclosure: Nothing to disclose

EP2185

The efficacy of non-invasive positive pressure ventilation for myotonic dystrophy type 1 in short and long-term

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Background and aims: Myotonic dystrophy is characterized by muscle and multiple organ dysfunctions. Respiratory failure related to life expectancy. However, there are few reports that examine the efficacy of non-invasive positive pressure ventilation (NIPPV) for myotonic dystrophy. We investigated the efficacy of this with blood gas analysis.

Methods: We recruited patients admitted to our hospital for myotonic dystrophy type 1 since 1993, using with NIPPV. We investigated the changes of blood gas analysis before and after that and longitude effects.

Results: There were 82 patients and 7 patients had been used NIPPV. The causes were one patient in CO₂ narcosis, one patient with pneumonia and 5 in the sensation of dyspnea. The mean of the partial pressure of arterial carbon dioxide (PaCO₂) before NIPPV is 59.0 Torr, the partial pressure of arterial oxide (PaO₂) is 66.8 Torr, the Base excess (BE) is 4.3, and pH is 7.35. After NIPPV, the mean of PaCO₂ is 54.9 Torr, PaO₂ is 75.0 Torr, BE is 4.1, and pH is 7.35. Four patients continued NIPPV after 1500 days. After 1500 days, the mean of PaCO₂ is 50.5 Torr, PaO₂ 70.8 Torr, BE is 2.0 and pH is 7.36. There was no significant difference between before and after NIPPV including after 1500 days. All case improved the symptom of dyspnea.

Conclusion: This study showed no adverse effect of NIPPV in myotonic dystrophy type 1. The tendency of decreasing BE might show improving respiratory acidemia with NIPPV.

Disclosure: Nothing to disclose

Neuroepidemiology

EP2186

Successful neurology trainee research network collaborative audit

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Background and aims: Successful Trainee Clinical Research Networks have been established since 2007. Our network in the peninsula, the SOUTHWEST Neurology Audit and Research Group (SONAR) is the first such Neurology trainee network in the UK. To enable development of cohesive collaborative working of the network we designed an audit which would be deliverable across three neurology centres within the peninsula.

Methods: We audited management of suspected acute meningitis and meningococcal sepsis against national guidelines within a 4-week period in December. A standardised anonymised data collation tool was used across the three centres and results were analysed at one centre.

Results: All 9 registrars on the rotation contributed to audit methodology design and data analysis; seven contributed cases (from all three centres). Ten cases were included in the audit, 6 (Exeter), 3 (Plymouth) & 1 (Truro). Our audit highlighted deficiencies in timely senior review, delivery of antibiotics and steroids, inappropriate administration of acyclovir and delay in lumbar puncture.



Conclusion: This was SONAR's first collaborative project and demonstrated that as a group of trainees we can successfully conduct a project across multiple hospital sites. We plan to extend the scope and ambition of our future undertakings.

Disclosure: Nothing to disclose

Patients



EP2187

Cancelled

EP2188

Six months as an emergency department neurologist in an University Emergency Hospital: A look back at referrals, diagnoses and admissions

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Background and aims: An Emergency Department (ED) neurologist has to deal with a plethora of diseases and symptoms, from the discomfort-causing benign ones to those posing a threat to the patient's life. We present a summary of the cases examined in our ED during 6 months in 2016.

Methods: We reviewed the logs from the Neurology ED from January 1st to June 30th 2016 and assessed the number of cases, the diagnoses and the percentage of patients admitted in the Department of Neurology for monitoring and treatment.

Results: A total of 7255 were examined by the ED neurologists, with an average of 39.86 patients per 24-hour shift. 1476 patients (20.34%) were admitted. Ischemic stroke (12.72% of total, 62.53% of admitted), transient ischemic attack (1.65% of total, 8.13% of admitted) and hemorrhagic stroke (1.16% of total, 5.69% of admitted) were the most common diagnoses. Out of the patients who weren't admitted, 1.020 (14.06%) had various types of headache, 954 (13.15%) vertigo and dizziness and 529 (7.29%) non-epileptic loss of consciousness; 1122 (15.47%) of the examined patients did not to have a neurologic cause for their presentation to the ED.

Conclusion: Poor referral and unnecessary presentation to the ED for diseases which can be managed in an outpatient setting significantly increase the workload for the ED neurologist and lead to inappropriate use of hospital resources. Better triage and systematic analysis of the ED logs can improve the quality of the medical care for real emergencies.

Disclosure: Nothing to disclose

EP2189

Clinical-epidemiologic aspects of myasthenia gravis (MG) in Georgia

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Background and aims: To investigate the data of MG distribution in Georgian territory – special with diversity of physical-geographic conditions.

Methods: Epidemiological aspects were studied in cities' and villages' population of East- and West-Georgia with various landscape areas. We used data of Georgian statistic department to calculate standard data. Investigation of epidemiologic aspects of MG conducted according to following data: sex, place of birth, place of living during disease manifestation, age of a patient during first signs of disease. We used for statistical evaluation SPSS 11.0.

Results: 365 MG patients were from 1931 to 2015: 55.8% - female, 44.2%-male, ratio 1.3/1. Age during the first signs of MG from 1 to 79, from that in 83.6% – between 16-60 years, until 40 years in 61.1% of women, 43.5% - men. The highest index of disease manifestation was 16-30 years in women, and 36-50 in men. The prevalence of MG per 100 000 in whole Georgian territory was – 3.1; East-Georgian – 3.4, West-Georgian - 1.9, in Tbilisi – 5.5, in city population – 4.0, village population – 1.5. According to physical-geographic areas MG is mainly distributed – in lowland and hilly regions, and practically not revealed in mountains' region. It should be noted, that lowland and hilly regions of Georgia are featured with dry climate and elevated mineralization of soil and underground waters.

Conclusion: The revealed higher prevalence of MG in cities' and some physical-geographic regions of Georgia confirm the opinion of several environmental factors has a high role in development of the disease.

Disclosure: Nothing to disclose

EP2190

Risk factors of cerebrovascular diseases and their impact on the development of acute vascular events: Epidemiological study in Belarus

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Background and aims: Significant differences in prevalence of cerebrovascular diseases (CVD) in the world are caused by variability of risk factors in different populations. The aim of study was to estimate the prevalence of risk factors of CVD and their influence on development of acute vascular events.

Methods: Screening of the open population of persons aged 40 to 59 years and dynamic monitoring after 1.5 and 3 years residing on the territory of one of districts of Minsk to identify risk factors of CVD. The following endpoints were evaluated: new cases of stroke, TIA or heart attack.

Results: 276 individuals were examined: 199 women (72%) and 77 men (28%). Mean age was 53±5.7 years. The most common risk factors in men were overweight, hypertension and smoking, in women - overweight, hypertension and hypodynamia. 1.5 years after screening dynamic observation of 270 patients was carried out, 71 patients - 3 years after. Six patients refused dynamic observation. During the observation, one case of stroke, one case of TIA and three cases of heart attack were recorded. Stroke and TIA was reported in women, and all cases of heart attack - in men. It was found out that all patients had a BMI ≥26, four of them suffered from not correctable hypertension, four - were burdened by family history of hypertension.

Conclusion: The findings indicate the need for in-depth study of CVD risk factors in specific populations and carrying out educational work among the population, which will contribute to the improvement of stroke prevention.

Disclosure: Nothing to disclose

EP2191

Characterisation of behavioural and psychological symptoms behind referrals to Dementia Units in patients with Alzheimer's disease

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Background and aims: Our goal is to evaluate whether the profile of behavioural and psychological symptoms (BPS) differs between Alzheimer Disease (AD) patients examined in Neurology Outpatient Clinics [NOC] and Dementia Units [DU].

Methods: This is an observational study that prospectively recorded data of 147 consecutive AD patients attended at NOC and 163 subjects with AD referred to DU in Spain (mean age at onset 75.3±6.7 years and mean duration of dementia 4.0±2.1 years, 67.8% women, Mini-Mental State Examination 15.8±6.4). The Neuropsychiatric Inventory (NPI) was used to assess BPS.

Results: At least one BPS occurred in 93.2% and 98.3% of AD participants evaluated in NOC and UD, the median NPI score was 48 and 36, with a median number of 4 and 6 symptoms per patient, respectively. The most frequent symptoms were depression (64.7%), anxiety (63.3%) and apathy (60.6%). In multivariate analysis, patients referred to DU had a higher risk of "clinically relevant" agitation [NPI ≥ 4] (OR:2.3, p=0.012), depression (OR:2.0, p=0.015), anxiety (OR:1.7, p=0.047), euphoria (OR:5.9, p=0.003), apathy (OR:2.9, p<0.001), disinhibition (OR:2.6, p=0.003), aberrant motor behaviour (OR:2.6, p= 0.001) and appetite/eating abnormalities (OR:1.8, p=0.024); and a lower risk of night-time behaviour disturbances (OR:0.29, p<0.001) than those attended at NOC.

Conclusion: In general, BPS are commoner in AD patients assessed in DU. That fact could be explained due to the diagnosis challenge that supposes the coexistence of affective symptoms in early stages and the management difficulties that involve hyperactive/frontal symptoms in all the stages of dementia.

Disclosure: Nothing to disclose

EP2192

Cancelled

EP2193

Cancelled

EP2194

Anxiety in patients with Parkinson's disease (PwPD)

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Background and aims: Anxiety is a common PD non-motor symptom. It's important that anxiety isn't simply reaction to the PD diagnosis instead a part of the disease itself, caused by changes in the brain chemistry. Estimates show that 25-45 percent of PwPD experience anxiety disorder [Joseph H. Friedman,2016]. Assessing PwPD anxiety profile is needed in Siberian region.

Methods: 798 PwPD are registered in movement disorders electronic database of the Siberian region. 269 PwPD were studied. Patients were clinically associated using neurologist-administered rating scales and self-administered questionnaires. Clinical assessments were conducted using the UPDRS, H&Y Scale, MoCA-test, Beck depression inventory II, Hospital anxiety and Depression Scale(HADS-A), Apathy Scale, PD Sleep Scale, Epworth Sleepiness Scale, Questionnaire for Impulsive-Compulsive Disorders in PD-Rating Scale(QUIP-RS), Bristol stool scale, Scale for Outcomes in PD for Autonomic Symptoms, Sniffing Stix Test, EuroQoL (EQ-5D), 39-item PD questionnaire (PDQ-39).

Results: Anxiety (65 men, 85 women) was diagnosed in 55.8%: 29.0% subclinical (78 PwPD: 40 women, 38 men), 26.8% clinically significant (72 PwPD: 45 women, 27 men). HADS-A score was negatively correlated with QoL scales and positively associated with apathy score ($r=0.300$, $p<0.0001$), depression severity ($r=0.436$, $p<0.0001$), QUIP-RS score ($r=0.321$; $p=0.004$), sleepiness ($r=0.205$; $p=0.005$), cognitive impairment ($r=0.203$; $p=0.005$). HADS-A scores weren't associated with onset age, illness duration, H&Y Stage, UPDRS scores. Generalized anxiety disorder, panic/phobic disorder, social phobia, agoraphobia, obsessive-compulsive and anxiety disorder not otherwise specified have been all identified in PwPD.

Conclusion: Anxiety can be even more disabling than the PD movement symptoms. It's important to recognize and treat it.

Disclosure: Nothing to disclose

Neuroimmunology 2

EP2195

Anti-MOG antibodies in a longitudinally extensive transverse myelitis after CMV virus infection

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Background and aims: Anti-myelin oligodendrocyte glycoprotein (anti-MOG) antibodies have been reported in different inflammatory disorders. The development of anti-MOG antibodies could be triggered by systemic infections but a clear association has not yet been established. We present a case with a longitudinally extensive transverse myelitis associated with anti-MOG antibodies, possibly triggered by Cytomegalovirus (CMV) infection.

Methods: A 41-year-old man had moderate fever during a primary CMV infection confirmed by significant increases in CMV IgM antibodies (8.04 Au/ml). Routine laboratory tests were within normal range. After a few days he developed symmetric progressive lower limb numbness and weakness with sphincter dysfunction. Neurological examination revealed a spastic paraparesis with lower trunk and limb hypoesthesia. MRI showed a spinal lesion involving C6-C7 and a longitudinally extensive lesion extended from T4 to the conus medullaris, with a slight enhancement at T4-T5 level after gadolinium administration. Cerebrospinal fluid (CSF) analysis, including CMV-PCR and serum anti-aquaporin 4 antibodies resulted negative.

Results: He fully recovered and had a five-year period of clinical stability. When the patient developed the onset of sexual disorders, anti-MOG antibody testing was performed and resulted positive (end point titre = 1:640). Considering the extent of the initial lesion, the new symptom and the antibody positivity, azathioprine was started.

Conclusion: This case highlights the possibility of an anti-MOG associated disease triggered by CMV infection. It is unknown whether this post-infectious entity is caused by mechanisms of molecular mimicry or failure of immunological tolerance towards anti-MOG antibodies.

Disclosure: Dr. De Rossi received speaker honoraria from Biogen and Teva and travel grants from Biogen, Teva and Merk Serono. Dr. Cordioli received consulting fees from Novartis and Merk Serono. Dr. Capra received consulting fees from Novartis, Biogen-Idec and lecture fees and/or travel grants from Novartis, Biogen-Idec, Genzyme and Sanofi-Aventis. Dr. Scarpazza, Dr. Mancinelli, Dr. Mariotto, Dr. Ferrari and Dr. Rasia have nothing to disclose.

EP2196

Acute necrotising encephalopathy syndrome: A rare cause of para-infectious encephalopathy in an adult

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Background and aims: We report a case of Acute Necrotising Encephalopathy Syndrome in an adult, and review the associated literature.

Methods: Case report.

Results: A 19-year-old man developed a febrile illness with cough, headache and progressive ataxia. On day 5 he collapsed without loss of consciousness, was incontinent of urine and subsequently unable to stand. Neurologically he was fully alert with signs of a spastic tetraparesis, however within one hour his GCS deteriorated to 8 and intubation was necessary. A Chest X-ray demonstrated consolidation throughout the left lung, and pneumococcal antigen was identified from urine. MRI brain demonstrated striking high-signal abnormalities involving the basal ganglia, midbrain and brainstem. CSF was unremarkable. The case met clinical and radiological criteria for Acute Necrotising Encephalopathy Syndrome (ANEC). The subsequent clinical course was in keeping with this diagnosis, with a prolonged period of spasticity and extrapyramidal signs associated with hyperpyrexia and deranged liver enzymes. There appeared to be a positive response to repeated plasma exchange and he fully recovered by 5 weeks.

Conclusion: ANEC is a rare para-infectious encephalopathy initially identified in East Asian children, but now recognised to occur throughout the world and occasionally in young adults. It can be distinguished clinically and radiologically from Acute Disseminated Encephalomyelitis (ADEM), its main differential diagnosis. The pathology also differs from ADEM, involving a 'cytokine storm' rather than inflammatory infiltration. We discuss the features of ANEC, its diagnostic criteria and proposed treatment. Although rare, this condition is almost certainly underdiagnosed, and earlier recognition may lead to more effective treatment.

Disclosure: Nothing to disclose

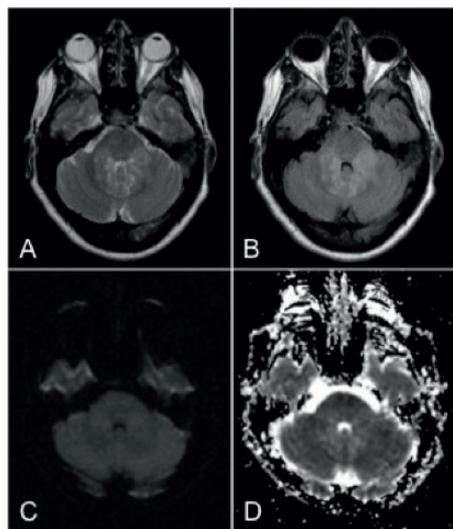
EP2197

Subacute brainstem syndrome compatible with CLIPPERS (Chronic Lymphocytic Inflammation with Pontine Perivascular Enhancement Responsive to Steroids)

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Background and aims: CLIPPERS was first described in 2010, comprising a subacute condition with brainstem clinical signs, punctate and curvilinear pontine enhancement on brain MRI and T lymphocytic infiltrate on histopathology. Clinical response to corticosteroids is observed, with frequent relapsing after treatment discontinuation. New clinical and imagiological presentations have been reported ever since, broadening the spectrum of CLIPPERS.

Methods: Case Report: A 47-year-old woman, with antecedents of in situ breast cancer in remission, presented with a 4-week history of progressing brainstem signs and symptoms. On neurological examination, hypoesthesia on the second territory of right trigeminal cranial nerve was first noticed. During the following month, the patient additionally developed ocular motility abnormalities and gait ataxia. Brain MRI disclosed multiple T2/FLAIR hyperintense lesions involving the pons, medulla and cerebellum. Subsequent MRI showed de novo bi-hemispheric hyperintensities involving the subcortical white matter. Cerebrospinal fluid analysis revealed CD19 lymphocytic pleocytosis, with no immunophenotypic atypia or evidence of B-cell monoclonality. Extensive differential diagnosis was excluded, making the diagnosis of CLIPPERS the most probable according to the established criteria. An optimal response to high-dose corticosteroids was observed, as expected in this entity. Three months after the first relapse, the patient remains asymptomatic and steroid free.



Brain MRI at clinical onset. (A) Axial T2-weighted (B) FLAIR (C) diffusion-weighted and (D) apparent diffusion coefficient map images obtained through. Diffuse patchy hyperintense lesions involving the pons, middle cerebellar peduncles, and bilateral medial cerebellum

hemispheres and vermis, without areas of diffusion restriction.

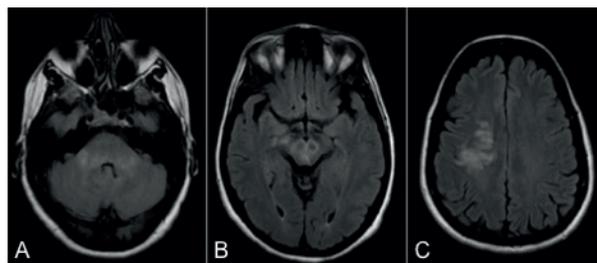


Fig. 2. Brain MRI 4 weeks after onset. (A) (B) and (C) Axial FLAIR images. Diffuse patchy hyperintensities at the pons and middle cerebellar peduncles. De novo lesions involving the mesencephalon and right centrum semiovale.

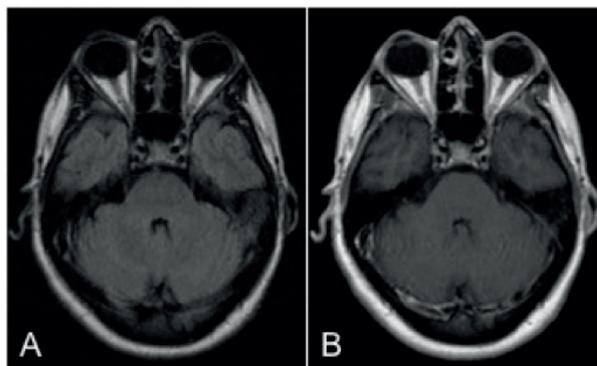


Fig. 3. Brain MRI after corticosteroid treatment and remission. (A) Axial FLAIR and (B) gadolinium T1-weighted images obtained through the level of the pons. Complete resolution of infratentorial lesions and no enhancement after gadolinium administration.

Results: NA

Conclusion: We report a case presenting with the clinical and neuroimaging features of CLIPPERS, according to recent literature. CLIPPERS is a diagnosis of exclusion, therefore a broad differential diagnosis must always be first considered. We underline the importance of a strict clinical and imagiological surveillance of these patients, in order to prevent incorrect diagnoses.

Disclosure: Nothing to disclose

EP2198

Cancelled

EP2199

MMP9 index as possible diagnostic marker of Neuro-Behçet's disease

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Background and aims: Neuro-Behçet's disease (NBD) is a neuroinflammatory disorder occurring in 5-30% of patients affected by systemic Behçet's disease (BD). NBD patients often show clinical and magnetic resonance (MRI) features "multiple sclerosis (MS) like" that make necessary a differential diagnosis from MS.

Methods: In this study we collected cerebrospinal fluid (CSF) and serum samples of 11 NBD and 21 relapsing remitting (RR) MS patients undergoing the diagnostic lumbar puncture. We measured the CSF and serum concentration of 18 soluble factors (MMP9, CXCL10, CXCL13, OPN, GM-CSF, TNF alpha, IFN gamma, IL-1 alpha, -1 beta, -2, -4, -6, -8, -10, -12p40, -12p70, -17, -23) by Milliplex.

Results: We found that NBD and RR-MS patients significantly differ about MMP9 content both in CSF and serum: NBD patients have a concentration of MMP9 lower in CSF ($p=0,002$) and higher in serum ($p<0,0001$) than RR-MS ones. By determining the ratio between CSF and serum MMP9 concentration and normalizing it versus CSF/serum albumin ratio, we defined the "MMP9 Index"; this parameter results significantly lower in NBD samples than RR-MS ones ($p<0,0001$). Furthermore, we detected a different CSF chemoattractant environment: higher IL8 amount in NBD and a higher CXCL13 amount in RRMS.

Conclusion: In conclusion, with this study we defined the "MMP9 index", that, if validated on an independent group of patients, could be proposed as a possible biomarker helpful to exclude the diagnosis of MS or to confirm the suspicion of NBD, especially in the cases of NBD positive for oligoclonal bands (OCB) (30% of NBD patients).

Disclosure: Nothing to disclose

EP2200

Safety of extended interval dosing of Natalizumab in clinical practice

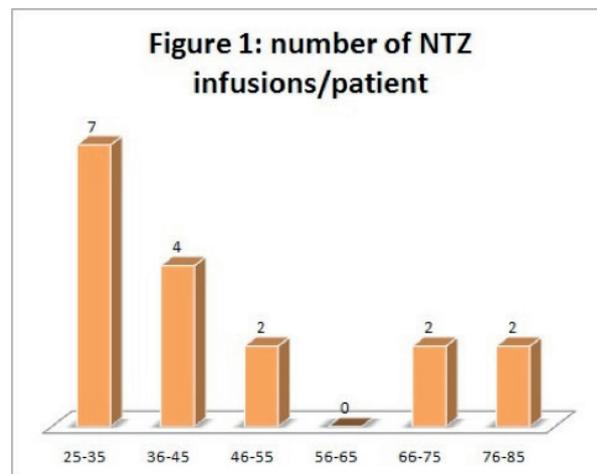
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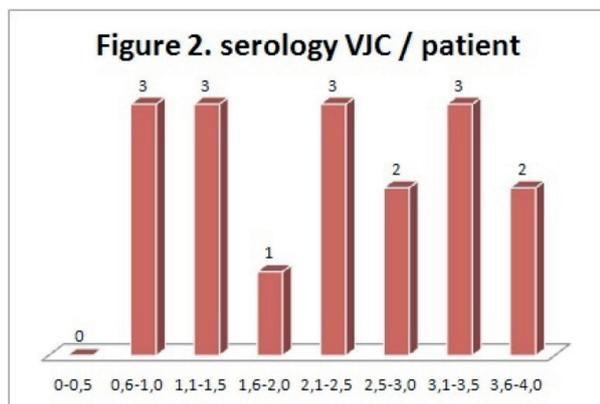
Background and aims: Natalizumab (NTZ) is a highly effective treatment for Relapsing-Remitting Multiple Sclerosis (RRMS), albeit associated with an increasing risk of progressive multifocal leukoencephalopathy (PML) in patients on treatment for over 24 months and who are seropositive for the JCV virus (PsJCV). NTZ is administered intravenously every 4 weeks, but clinicians have been extending infusion intervals in the attempt of reducing PML risk. This study aimed to evaluate the safety of extending interval dosing (EID) of NTZ from 4 to 5 weeks in our clinical practice.

Methods: We performed EID on clinically stable RRMS NTZ-treated patients with PsJCV (index $\geq 0,9$) and >24 infusions. A retrospective review of all cases undergoing EID was conducted in 2016. Age, sex, disease duration, total NTZ-treatment time, clinical relapses, lesion load and EDSS progression were analyzed and compared with those occurring in the same group of patients in the year before EID.

Results: Seventeen patients were identified: 11 women (64.7%) with a mean age of 43.17 (± 8.76), mean EDSS of 2.29 (± 1.19), average disease duration of 10.76 years (± 4.25), average NTZ-treatment time of 5 years (± 2 years) and mean follow-up on EID of 8.4 months (± 6.2). EID was not associated with clinical relapses, increasing lesion load or EDSS progression. No cases of PML were registered.



Number NTZ infusions/patient



Serology vJC/patient

Conclusion: In our cohort EID did not compromise treatment outcomes. EID could be an option for maintenance therapy for patients on NTZ. Prospective studies are warranted to determine if the risk of PML is reduced in patients on EID.

Disclosure: Nothing to disclose

EP2201

Features of electroneuromyographic (EMG) diagnosis of paraneoplastic polyneuropathy (PPNP) in patients with small cell lung cancer (SCLC) who are seropositive for anti-CV2 antibodies

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Background and aims: PPNP one of the most common types of the course of paraneoplastic neurological syndrome. The most commonly it is encountered in SCLC. We study the features of EMG diagnostics of PPNP in patients with SCLC who are seropositive for anti-CV2 antibodies.

Methods: We examined 12 patients of the main group (MG) with SCLC morphologically confirmed (mean age 51.8 ± 12.8) and 20 patients of the control group (CG) (mean age 53.1 ± 6.8). Two groups of patients were examined neurologically, electroneuromyographically (nerves of the upper and lower extremities - motor and sensory fibers of the median, ulnar and peroneal nerves). Laboratory diagnostics by immunoblot (euroimmune) on paraneoplastic onconeural antibody revealed that all patients of MG were seropositive on anti-CV2(CRMP5) antibodies.

Results: When comparing the EMG amplitude performance and speed of median (SMN), ulnar (SUN) and peroneal nerves (SPN) through sensory fibers of patients of MG and CG statistically significant differences were revealed ($P=0,05$). The amplitude and speed of the SMN of MG - $4.4 \pm 2.7 \mu V$ $44.5 \pm 7.2 m/s$; CG - $7.3 \pm 0.4 \mu V$, $57.4 \pm 4.2 m/s$; amplitude and speed of SUN of MG - $7.1 \pm 1.9 \mu V$ and - $41.5 \pm 7.1 m/s$; CG - $15.4 \pm 6.8 \mu V$ and $56.2 \pm 6.4 m/s$; amplitude and speed of SPN of MG - $4.4 \pm 2.7 \mu V$, $40.5 \pm 7.2 m/s$; CG - $7.4 \pm 0.4 \mu V$, $57.4 \pm 4.2 m/s$.

Conclusion: The patients with SCLC who are seropositive on anti-CV2 (CRMP5) antibodies develop sensory axonal-demyelinating paraneoplastic polyneuropathy.

Disclosure: Nothing to disclose

EP2202

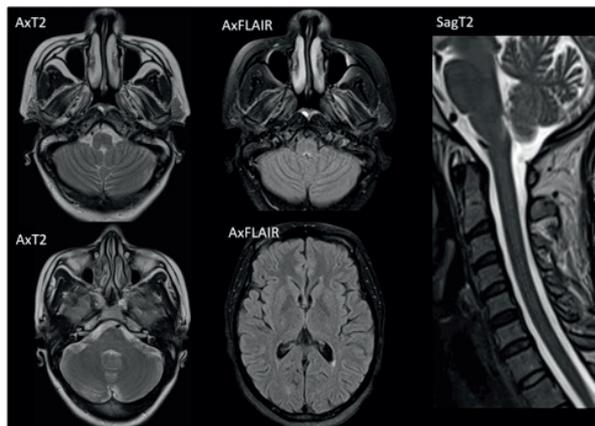
Anti-aquaporin 4 IgG positive Neuromyelitis Optica with an atypical presentation

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Background and aims: Neuromyelitis Optica (NMO) is an astrocytopathy associated with anti-aquaporin 4 antibodies, classically characterized by severe relapses of optic neuritis (ON) and longitudinally extensive myelitis with poor recovery.

Methods: Case report

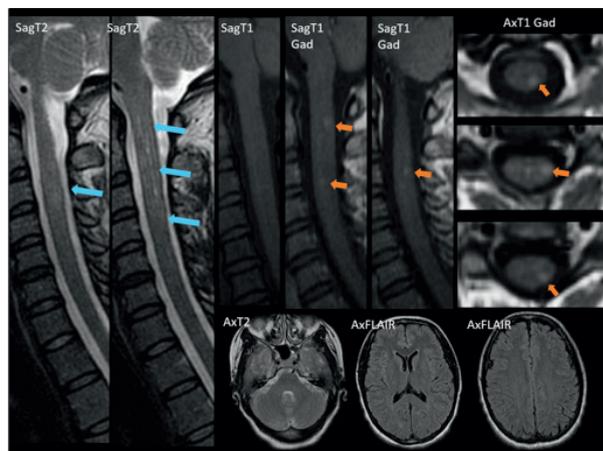
Results: Thirty seven-year-old black woman admitted in 2010 for paroxysmal dysesthesia involving progressively the right lower limb, torso and homolateral upper limb and lower left limb, in the previous three months. Neurological examination showed lower limbs hypopalessthesia. MRI disclosed heterogeneity of C1-C4 spinal cord signal, with T2 hyperintense areas, without T1 hypointensity, mild spinal expansion and mild enhancement after gadolinium, suggesting a demyelinating or tumoral lesion; brain MRI was normal. CSF cytochemical analysis, oligoclonal bands and screening for infectious/systemic autoimmune diseases were unremarkable. Symptomatic remission under pregabalin. In 2012, right ON, with compatible MRI, without new brain lesions and normal spinal exam (disappearance of the signal change previously described). In the following months, left ON and right ON, without recovery of right eye vision after methylprednisolone. Despite an initial negative investigation (anti-AQ4 and anti-MOG antibodies), anti-AQ4 IgG were detected at this stage. Clinical stability was achieved with AZA and PRD for three years. Recently, area postrema syndrome (poor therapeutic compliance), with total recovery with methylprednisolone, without new MRI lesions.



MRI performed 11 days after methylprednisolone for area postrema syndrome without new brain lesions and normal spinal exam.

Conclusion: We present a case of NMO spectrum disorder with anti-AQ4 IgG with a mild clinical presentation: paroxysmal symptoms associated with spinal cord lesion with atypical behavior - spontaneous resolution without subsequent atrophy. The expanding NMO phenotype includes mild ON and myelitis as manifestations, highlighting the importance of systematic screening for anti-AQP4 IgG.

Disclosure: Nothing to disclose



Spine MRI: heterogeneity of C1-C4 spinal cord signal, with T2 hyperintense areas, without T1 hypointensity, mild spinal expansion and mild enhancement after gadolinium. Brain MRI was normal.

EP2203

Immunological reactivity in children with stroke

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Background and aims: Knowledge of the characteristics of stroke in children is necessary for the diagnosis, treatment and preventive care. Undoubtedly, in pathogenesis of stroke an important role plays immunological mechanisms.

Objectives: to study the immunological and autoimmune reactivity of children after stroke.

Methods: 74 children examined, 44 aged under 3 years in the acute and chronic phases of stroke and 30 healthy children at the same age. The levels of cytokines were detected by immunoenzyme method using commercial test kits "Vector-Best" (IL-1beta, IL-10). The sensitivity of the method was 2-30pg/mL. We analyzed the ANCA (Anti-neutrophil cytoplasmic antibodies) level to evaluate the general condition of the vascular system.

Results: The main pro-inflammatory cytokine IL-1beta levels in main group increased significantly ($P < 0.001$) reaching an average level of 103.3 ± 0.9 pg/mL, while in the control group, averaged 29.9 ± 1.8 pg/mL. The level of IL-10 in the main group was slightly reduced (12.9 ± 1.0), but the difference was not reliable ($P > 0.001$) compared to the control group. ANCA level was 0.962 ± 0.056 standard units, which is 3 times higher than in the control group and indicates the inflammatory process in the intima.

Conclusion: Immune reactions and related local inflammation involved in the pathogenesis of stroke and infarct changes in human brain tissue. Not only the excess releasing of proinflammatory cytokines like IL-1beta, but the deficit of anti-inflammatory cytokines like IL-10 plays important role in the development of inflammatory response. High levels of ANCA and IL-1beta has an unfavorable prognosis for a disease course.

Disclosure: Nothing to disclose

EP2204

Cancelled

EP2205

Bickerstaff brainstem encephalitis and Miller-Fisher syndrome - A recurrent case of ophthalmoplegia, ataxia and areflexia

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Background and aims: Guillain-Barré syndrome, Miller-Fisher syndrome (MFS) and Bickerstaff brainstem encephalitis (BBE) comprise a spectrum of the same immune-mediated disease, entitled anti-GQ1b antibody syndrome. While they are typically monophasic, a limited number of recurrent cases has been reported, usually similar to the inaugural episode.

Methods: Case report.

Results: A 63-year-old male presented with diplopia, unsteadiness, dysesthesia and dysphonia, following a respiratory tract infection. He had prominent truncal and appendicular cerebellar ataxia, generalized areflexia and nearly complete ophthalmoplegia. He also developed mild tetraparesis, distal proprioceptive deficits, nearly abolished vibration sense, left blepharoptosis, right relative afferent pupillary defect and bulbar palsy. A left Babinsky sign was noticed. Cerebrospinal fluid analysis and brain magnetic resonance imaging (MRI) were performed and were irrelevant. Electromyography exhibited low amplitude sensory nerve action potentials, F-waves' chrono-dispersion in the median nerve and abolished H reflexes. He was diagnosed with MFS and he underwent immunoglobulin therapy, with favorable outcome. Six years earlier, following mixed pollen extract immunotherapy, he developed ophthalmoplegia, ataxia, areflexia, with altered mental status and diminished vibration perception in the left side of his body. Anti-GQ1b antibody was noticeably elevated. Electromyogram revealed a sensory-motor polyneuropathy. Brain MRI was unspecific. MFS was assumed, and after treatment with intravenous immunoglobulin, plasmapheresis and steroids, complete recovery was attained.

Conclusion: It is our view that this patient suffered a first episode of BBE, and now presents to our care with MFS. Such cases of recurrent anti-GQ1b syndrome under different phenotypes are exceedingly rare, and whether genetic susceptibility mechanisms exist is still unclear.

Disclosure: Nothing to disclose

Neuro-ophthalmology/ neuro-otology

EP2206

Male idiopathic intracranial hypertension: A different entity? A 12-year tertiary centre experience

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Background and aims: Idiopathic intracranial hypertension is typically seen in females with high body mass index. The diagnosis of IIH in males must only be made after an extensive search for secondary causes of raised intracranial pressure. We have retrospectively reviewed the clinical characteristics and prognosis of male IIH at our centre.

Methods: We reviewed the notes of 14 men fulfilling the modified Dandy criteria for IIH, diagnosed under our services at University Hospitals of Leicester between 2004-2016.

Results: The case series included 14 male patients aged between 17 and 85 years old. BMI range was 23 to 43kg/m². 14% (n=2) of the patients presented with headache only, 43% (n=6) presented with vision changes only and 43% (n=6) presented with headache plus vision changes, 14% (n=2) patients reported tinnitus, 43 (n=6) patients required surgical intervention, of which 36% (n=5) had optic nerve fenestration, 7% (n=1) had ventriculoperitoneal (VP) and 14% (n=2) had lumbar theco-peritoneal (LP) shunt. Of the patients requiring surgical intervention, 50% (n=3) still had deterioration of their visual function. 60% (n=3) of patients having optic nerve fenestration also required a second surgical procedure (ventriculoperitoneal or lumbar theco-peritoneal shunt). On follow-up, 57% (n=4) of the patients originally presented with headache, reported resolution of this.

Conclusion: The commonest clinical presentation was visual impairment 86% (n=12), followed by headache 50% (n=7). There was a trend for our male cohort to be older, with disproportionately greater risk of severe visual loss and a higher proportion requiring surgical intervention. The findings suggest that males with IIH may require close monitoring and timely intervention in tertiary centres to avoid poor visual outcomes.

Disclosure: Nothing to disclose

EP2207

Risk factors and prognosis in isolated ischemic ocular motor cranial nerve palsy

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Background and aims: Ischemic isolated ocular motor cranial nerve palsies are frequent in older and has been related with the presence of diabetes, hypertension and other risk factors. There are not previous studies to study the relationship between the presence of risk factors with the time to complete recovery.

Methods: Describe our serie of patients with isolated ocular cranial nerve ischemic palsy and investigate the vascular risk factors and the relationship with recovery time. Patients with third, fourth and sixth cranial nerve ischemic palsies treated at our Unit. Demographic data were collected, as well as cardiovascular risk factors (arterial hypertension, dyslipemia, smoking and ischemic heart disease) and time to recovery. Patients were divided into two groups depending the time to recovery (>3 or <3 months). we analyze the possible relationship between the recovery time and the presence of each risk factor.

Results: 48 patients with an average age 67.83 at diplopia onset. 11 (24.4%) developed a third nerve palsy (np), 2 (4.4%) a fourth np, and 35 (77.7%) a sixth np. Hypertension, diabetes mellitus and hyperlipidemia were significantly more prevalent than ischemic heart disease and smoking. In multivariate analysis we found a relationship between diabetes and time to recovery, longer in diabetics patients.

Conclusion: Ischemic ocular motor nerve palsy is the main cause of isolated cranial nerve palsy in adults. In our serie all patients were older than 50 and have at least one vascular risk factor. In our knowledge there are no previous data about the link between diabetes and time to recovery.

Disclosure: Nothing to disclose

EP2208

Cancelled

EP2209

From Miller-Fisher syndrome to functional convergence spasm

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Background and aims: Functional disorders may resemble many neurological disorders with a difficult diagnosis in some cases.

Methods: A 56-year-old male with no personal data of interest was admitted in May 2015 due to a slight instability. Brain CT was normal. The patient progressively developed an abduction disturbance in the left eye on looking to the left, an abduction disturbance in the right eye on looking to the right, and a limitation on vertical gaze with convergence spasm. He presented instability but preserved reflexes. A complete neurological and systemic study was done and was normal. The patient received intravenous immunoglobulins experiencing an aseptic meningitis as adverse event. The patient was discharged home with a diagnosis of probable Miller-Fisher syndrome. At follow-up, the patient was able to carry out all normal activities (including working, writing and driving) but neurological status still showed a convergence spasm. In addition to neurological disorder, systemic complains such as cardiological and digestive disorders were also studied and revealed normal results. A clinical improvement was seen under antidepressive treatment.

Results: Characterized by intermittent episodes of convergence that may mimic abducens paresis, converge spasm has not been well characterized, and may often be misdiagnosed by neurologists as brainstem pathology. In our patient a complete study was performed, and only a correct diagnosis was done at the follow up. Functional converge spasm often coexist with other psychogenic disorders.

Conclusion: The prompt awareness of detecting this syndrome may lead to an early correct clinical approach and avoid unnecessary diagnostic and invasive studies.

Disclosure: Nothing to disclose

EP2210

Positional nystagmus of central origin due to cerebellar PICA infarctions

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Background and aims: Brainstem and cerebellar infarctions may cause acute vertigo, often mimicking vestibular neuritis. In contrast, attacks of positional vertigo mostly reflect benign paroxysmal positional vertigo (BPPV), but may rarely be of central „pseudo-vestibular“ origin, as the following cases show.

Methods: Case reports: Two females and one male patient were admitted because of acute attacks of severe positional vertigo, associated with nausea and omnidirectional ataxia of stance and gait.

Results: Case 1 (female, age 38) showed leftward saccadic smooth pursuit, but no pathological nystagmus. MR imaging revealed right cerebellar infarcts in the right PICA and SCA territories. Case 2 (female, age 71) presented with non-habituating ageotropic positional nystagmus with severe vertigo, further periodically alternating horizontal spontaneous nystagmus, obeying Alexander's law, due to acute left PICA infarction. Videonystagmography showed mildly reduced caloric excitability of the left labyrinth, the video head impulse test bilaterally reduced VOR gain. Case 3 male, age 68) developed persistent mild nausea and ageotropic positional nystagmus with vertigo. MR imaging showed right cerebellar PICA infarcts, due to V4 occlusion.

Conclusion: Our cases show that pseudo-vestibular infarctions in the PICA territory may be symptomatic by central positional vertigo with or without nystagmus. It often beats in ageotropic direction, similar to cupulolithiasis of the horizontal canal. Its central origin may be indicated by discrete clinical signs such as bilateral gaze-evoked nystagmus, saccadic smooth pursuit, missing habituation of positional nystagmus, which may also have a bad correlation with the intensity of vertigo. MR imaging should be initiated, even with pathological head impulse test.

Disclosure: Nothing to disclose

EP2211

Acute binocular double vision

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Background and aims: Acute binocular double vision is a diagnostic challenge in the emergency room and is most commonly due to extraocular nerve palsies. A precise clinical and etiological classification at first medical contact is of utmost importance for promptly taking the correct therapeutic decision.

Methods: We prospectively evaluated 54 patients (age 59.2±16.7 yrs) that presented to our emergency room with acute binocular double vision (no longer than ten days). Personal history was taken on the basis of a standardized questionnaire. Patients underwent a thorough neurological and neuro-orthoptical examination, including evaluation of ocular torsion using scanning laser ophthalmoscopy, subjective visual vertical (SVV) and harms target screen test. Brain-MRI with was performed in all but five patients.

Results: Forty-six patients (85%) were diagnosed with an extraocular nerve palsy (26% NIII, 17% NIV and 43% NVI), two patients with an isolated extraocular muscle paresis, three with a vertical (skew) deviation, two with an internuclear ophthalmoplegia and one patient with a decompensated strabismus deorsoadductorius. The subjective visual vertical changed independently on both eyes according to the site of lesion (peripheral vs central). On the basis of the clinical findings and SVV changes in the paretic and normal eye, we developed a clinical diagnostic algorithm.

Conclusion: A systematical approach to acute, binocular double vision, especially when taking into account the subjective visual vertical on both eyes can help guide clinicians to differentiate peripheral from central lesions accurately.

Disclosure: Nothing to disclose

EP2212

Ophthalmic findings in CANVAS syndrome

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Background and aims: Cerebellar Ataxia, Neuronopathy, Vestibular Areflexia Syndrome (CANVAS) was recognised as a distinct clinical syndrome in 2011. Afferent visual system abnormalities are a common feature of other ataxias. We set out to characterise ophthalmic involvement in CANVAS

Methods: 16 patients with clinical diagnosis of CANVAS were compared with 15 healthy controls A Complete neuro-ophthalmic examination was performed including an optical coherence tomography (OCT) examination of peripapillary retinal nerve fibre layer (RNFL) and macula Patients'neurological impairment was rated on the Scale for the assessment and rating of ataxia (SARA)

Results: There were no significant differences in demographics between cases and controls. (Figure 1) Visual acuity was worse and cup-to-disc ratio was greater in cases compared with controls (Figure 1) While overall average Retinal Nerve Fibre Layer was the same in cases and controls the temporal RNFL was thinner in patients than controls. (Figure 2) Total macular volume was increased and this was apparent all sectors but particularly in the outer macular regions, especially nasally. No association was seen between OCT findings and SARA ataxia scores.

Results

	CANVAS Patients (SD), N=16	Healthy Controls (SD), N=15	p Value
Age (years)	65.4 (8.6)	62.1 (6.9)	0.24
Female gender	11/16 (68.7%)	9/15 (60%)	0.26
Visual acuity (logMAR)	0.17 (0.15)	0.00 (0.04)	0.0002
Intraocular pressure	15.4 (3.2)	15.1 (2.0)	0.77
Cup to disc ratio	0.51 (0.16)	0.37 (0.11)	0.01
SARA score (/40)	12.8 (6.1)	-	
Symptom duration (years)	13.4 (8.5)	-	
Age at symptom onset (years)	51.9 (9.0)	-	

Figure 1. Demographics

Results

	CANVAS Patients (SD), N=9	Healthy Controls (SD), N=15	p Value
RNFL Thickness			
Average RNFL	92.8 (7.2)	96.6 (8.5)	0.27
Superior RNFL	111.9 (12.7)	117.1 (14.5)	0.38
Nasal RNFL	77.4 (12.3)	73.2 (12.5)	0.42
Inferior RNFL	123.3 (12.8)	124.0 (17.1)	0.91
Temporal RNFL	58.8 (6.1)	71.7 (11.6)	0.005

Figure 2. Optic Coherence Tomography measurements of the Retinal Nerve Fibre Layer

Conclusion: The observed decreased in Visual acuity is

likely to be due to nystagmus

The Temporal RNFL thinning in CANVAS may suggest mitochondrial dysfunction as mitochondrial diseases show a similar pattern of change. The cause of the thickened macular is uncertain. This is a small preliminary study which is not surprising given that the condition is relatively rare. Further investigation into these OCT findings will be of interest

Disclosure: Nothing to disclose

EP2213

Examination of upright posture instability in senior patients by posturography with sensory tests

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Background and aims: Impairment of upright stance is very common in senior patients and strongly influences their quality of life. The causes of disequilibrium can be very different and often present a challenge in diagnostics... The aim of the presented work is to examine the contribution of static posturography in evaluation of instability in senior patients.

Methods: In the years 2013-2014 we examined 230 of the senior patients (over age of 65y). We performed posturography with sensory tests (galvanic vestibular stimulation, unilateral vibration of Achilles tendon). We evaluated the velocity and amplitude of body sways, total area, as well as frequency analysis was done

Results: Posturographic tests were able to quantify the extent of instability of patients and also to define the different characteristics of upright posture impairment. Patients with somatosensory disorders (i.e. polyneuropathy) showed increased velocity and an increase of frequencies above sways points 1Hz in the anterior-posterior direction. Patients with diffuse cerebral white-matter lesions were characterized predominantly with increased body sways amplitude and with pronounced response to sensory stimulation. Patients with vestibular disorder were often unable to maintain a stance on soft (foam) platform. They showed asymmetrical responses to the galvanic vestibular stimulation and the improvement of stability in head-extension posture

Conclusion: Disorders of upright stance are very frequent in senior patient and usually several factors contribute to the impairments of stance... Static posturography is a useful method for detection of dominating cause of instability in senior patients.

Disclosure: Nothing to disclose

EP2214

Clinical characteristics of recurrent vestibulopathy: Clearly distinctive from vestibular migraine and Menière's disease?

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Background and aims: We aimed to systematically investigate the clinical characteristics of recurrent vestibulopathy (RV), Vestibular Migraine (VM) and Menière's Disease (MD). The second objective was to assess whether clinical symptoms existed that were unique to RV discriminating it from VM and MD.

Methods: Between January 2015 and November 2016, patients were prospectively recruited at a specialised dizziness unit. Patients were included if they met the diagnostic criteria for either RV, VM or MD. The clinical diagnosis was based on mutual consensus after consultation of an ENT-surgeon and a neurologist.

Results: A total of 122 patients were included, 65 (53%) were females in whom 29 (24%) were postmenopausal. The mean age was 55.5±13.7 years and the mean age of onset of vertigo attacks was 49.2±14.8 years (n=119). Forty-five (37%) patients had a clinical diagnosis of RV, 18 (15%) of pVM, 16 (13%) of dVM and 43 (35%) of MD. Clinical symptoms in these three vertigo disorders were comparable and no symptom could be identified which was specifically linked to RV. Patients with VM reported significantly more often a positive history of motion sickness. In addition, canal paresis was most profound in patients with MD.

Conclusion: We state that no clinical characteristics could be identified which were distinctive for RV. Nonetheless, we did find several distinctive clinical features for VM and MD which may assist the physician in his history taking. Prospective long-term might contribute to the discussion of whether or not RV can be identified as a separate clinical entity.

Disclosure: Nothing to disclose

Peripheral nerve disorders 2

EP2215

Effects of smart phone use on the median nerve

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Background and aims: We can understand the importance and the popularity of smart phones when we evaluate their sales. The median nerve is the main responsible nerve for the muscle movements while using smart phones (Fig 1). Various reasons; particularly frequent repetitive movements can lead to carpal tunnel syndrome (CTS) via median nerve damage. The aim of this study is to evaluate the effects of smart phone usage on the median nerve.

Methods: In this study, the sampling group was composed of 40 smart phone users and 22 classical mobile phone users (totally 62 individuals). The use of smart phone was assessed by using smart phone addiction scale (SAS). Participants were divided into three groups; high smartphone users (SAS >71), low smartphone users (SAS <71) and classical mobile phone users. In order to evaluate the upper extremity functions and symptoms, quick-disabilities of arm, shoulder, hand (qDASH) survey was applied to participants. Participants were also assessed by using visual analogue scale (VAS). Electrophysiological examination was performed by using Micromed SpA device.

Results: Totally 62 participants were included in the study. The 37 of the participants (57.9%) were female and 25 of them (40.3%) were male.

Table 1. Demographic and electrophysiological datas of participants

	Classical cell phone	Low smartphone	High smartphone	P
	users (n=22)	users (n=19)	users (n=22)	
VAS pain (cm)	2,95 ± 2,01	2,15± 2,16	2,90 ±1,92	0,15
Q-dash score	16,63 ± 13,92	13,26± 10,74	19,80± 12,74	0,30
MN SCV	52,91 ± 4,69	60,62 ± 4,42	50,77± 9,24	0,00
MN SL	2,74 ± 0,37	2,28 ± 0,22	3,01± 0,62	0,00
MN MCV	54,38 ± 6,42	58,24± 3,53	51,93±6,32	0,03
MN ML	3,31±0,41	2,90± 0,34	3,55±0,55	0,00

Datas are mean±standard deviation. P-values are from analysis of Kruskal–Wallis tests. VAS, visual analogue scale; Q-dash, Quick-Disabilities of Arm, Shoulder, Hand score; MN, median nerve; SCV, sensory conduction velocity; SL, sensory latency; MCV, motor conduction velocity; ML, motor latency

Table 2. Comparison of dominant and non-dominant hand electrophysiological datas

	Dominant-side	Non-dominant side	P
Classical cell phone users (n=22)			
MN SCV	52,91±4,69	56,78±5,38	0,03
MN SL	2,74±0,37	2,43±0,25	0,02
MN MCV	54,38±6,42	58,00±4,59	0,01
MN ML	3,31±0,41	3,02±0,43	0,00
Low smartphone users (n=19)			
MN SCV	60,62±4,42	60,01±6,28	0,74
MN SL	2,28±,22	2,24±,22	0,22
MN MCV	58,24±3,53	58,61±5,40	0,77
MN ML	2,90±,34	3,06±,36	0,07
High smartphone users (n=22)			
MN SCV	50,77±9,24	57,01±6,37	0,00
MN SL	3,01±,62	2,43±,25	0,00
MN MCV	51,93±6,32	59,04±4,23	0,00
MN ML	3,55±,55	3,23±,47	0,06

Datas are mean±standard deviation. P-values are from analysis of Mann-Whitney U test. MN, median nerve; SCV, sensory conduction velocity; SL, sensory latency; MCV, motor conduction velocity; ML, motor latency

Conclusion: In our study, median nerve sensory, motor conduction velocity, and differences in latencies were examined. It was observed that smart phone usage rarely influenced median nerves according to the classical mobile phone usage. However, median nerves were adversely affected by the increasing use of smart phones.

Disclosure: Nothing to disclose

EP1213

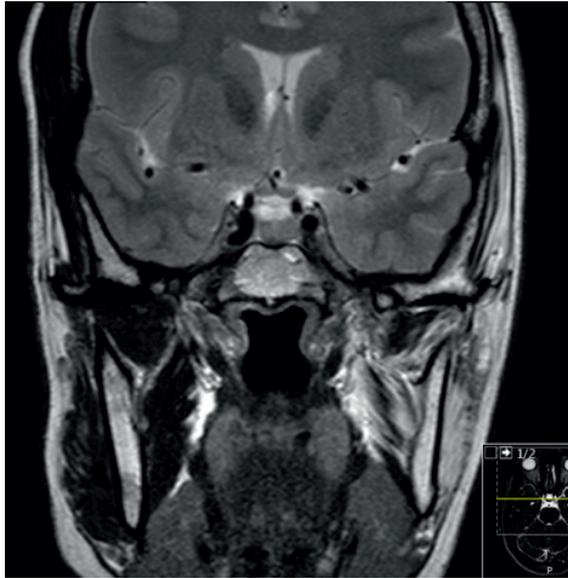
A rare cause of facial asymmetry

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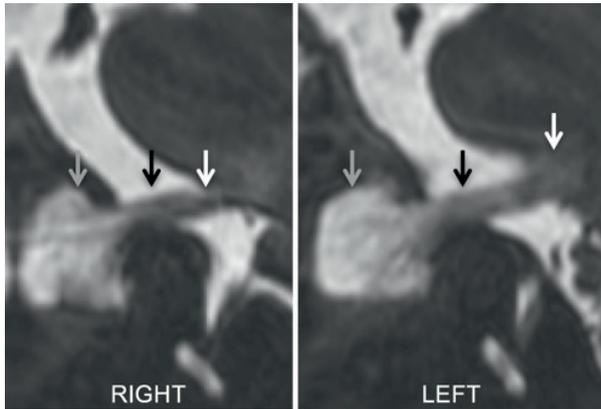
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Background and aims: We report a patient presenting with facial asymmetry due to isolated unilateral trigeminal motor neuropathy.

Results: A 40-year-old woman presented with progressive facial asymmetry, left hemifacial numbness and pain for the last month. She denied past history of head or facial trauma, dental procedures, diabetes herpes-zoster or other infections, as well as systemic symptoms. On neurological examination it was disclosed left temporal and masseter muscle atrophy, left deviation of the mandible on opening of the mouth, and mild poorly-defined left hemifacial hypoesthesia. Electrophysiological study confirmed the diagnosis of pure motor trigeminal neuropathy, with chronic neurogenic potentials in the atrophic muscles. Trigeminal sensory fibers were normal on blink reflex and facial laser-evoked potential. Facial and cranial MRI revealed atrophy and fatty infiltration on left masticator muscles (figure 1) and regular thickening of the affected fifth cranial nerve at its origin in the anterolateral surface of the pons, extending to cisternal portion and Meckel's cave (figure 2), which suggested an inflammatory lesion. Blood and cerebrospinal fluid studies were negative for autoimmune and infectious diseases. Clinical picture remained stable over 9 months of follow-up.



Facial MRI coronal. Fat infiltration on left masticatory muscles



Cranial MRI, T2 3D DRIVE HR, reformatted images along the trigeminal nerves. Thickening and hyperintense signal on apparent origin (white arrows), cisternal segment (black arrows) and Meckel's cavum (gray arrows) of the fifth cranial nerve.

Conclusion: Trigeminal neuropathy is usually characterized by motor and sensory involvement. Reviewing the literature we found that 16 similar cases have been reported. As described in some other patients, sensory symptoms were referred in spite of isolate motor involvement on neurophysiology investigation. There is a wide array of possible etiologies for this neuropathy, however in most of the cases, no apparent cause is found.

Disclosure: Nothing to disclose

EP1214

Bilateral carpal tunnel syndrome as an adverse effect of Pembrolizumab

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Background and aims: Pembrolizumab is a monoclonal antibody approved for treatment of metastatic melanoma and non-small cell lung cancer. We report a case of acute bilateral carpal tunnel syndrome as a possible adverse effect to Pembrolizumab.

Results: A 77-year-old man presented with progressive paresthesia and numbness in fingers and hands for the last month. Five months before he had started treatment with Pembrolizumab 2mg/kg IV every three weeks for metastatic melanoma. He denied similar symptoms on the past. He rejected recent repetitive manual activity, distal edema or arthritis symptoms. On neurological examination it was disclosed bilateral positive Phalen sign and hypoesthesia in median nerve territory. Nerve conduction studies confirmed severe bilateral carpal tunnel syndrome, without signs of peripheral neuropathy. Bilateral carpal infiltration with betamethasone dipropionate and levobupivacaine was performed, with major symptomatic and electrophysiological improvement over the following week. Pembrolizumab treatment was continued and three months later he remains clinically well, with continued neurophysiological recovery.

Conclusion: This is the first report of bilateral carpal tunnel as an adverse reaction to Pembrolizumab. One of the possible mechanisms could be a bilateral tenosynovitis of the wrist, as this condition has been reported as an uncommon adverse reaction to this drug. In our patient we found a segmental demyelization, in a local prone to nerve compression, as the most probable explanation.

Disclosure: Nothing to disclose

EP2216

Clinical and diagnostic aspects of sensory polyneuropathy in obese patients with impaired glucose

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Background and aims: Sensory neuropathy is a marker of preclinical lesions of the nerves in diabetes mellitus and prediabetes

Methods: We examined 46 patients aged from 28 to 65 years (50.32±4.4 years) with obesity, diabetes mellitus (DM) type 2 (disease duration of 5.33±3.16 years), impaired fasting glucose, impaired glucose tolerance. The obesity of the first degree was observed in 19 people (41.3%), second degree - in 22 (47.8%), third degree - in 5 (10.9%) patients rves in diabetes mellitus and prediabetes

Results: Sensory neuropathy diagnosed in 34 (74%) patients with obesity and glucose impairments. The main complaints of patients were pain, numbness and cramps in the legs, worse at night, that were observed in 68%, 15% and 17% cases respectively. The clinical symptoms in 82.4% of cases were confirmed by the results of the quantitative sensory testing. Clinical manifestations of sensory fibers lesions were more frequently detected in patients with prediabetes (80%). In patients with obesity without glucose disorders the prevalence of neuropathy was 68%, with severe polyneuropathy in 6 (46.1%) of them. In group with DM type 2 the diabetic polyneuropathy was detected in 75% of the patients, the most frequently (38.4%) it was mild polyneuropathy

Conclusion: Our data demonstrate the possibility of early development of sensory polyneuropathy in patients with obesity and prediabetes before the laboratory and clinical manifestation of DM type 2, and its progression with chronic hyperglycemia

Disclosure: Nothing to disclose

EP2217

Sural, ulnar sensory responses and sural/ulnar amplitude ratio (SUAR) in varying age group: Influence of age on nerve conduction

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Background and aims: In electrodiagnostic studies, age is probably the most significant variable, with sensory response amplitudes declining progressively with advancing age. Our purpose is to determine the lower limit of the normal value (LLN) for sural and ulnar SNAP amplitudes as well as for the SUAR at varying ages and confirm the hypothesis that the SUAR is independent of age.

Methods: The subject population was divided into four age groups: group 1: ≤39, group 2: 40-59, group 3: 60-69, and group 4: ≥70. All subjects were performed sensory nerve studies on ulnar (finger-to-wrist), sural nerves. The sural/ulnar SNAP amplitude ratio was calculated.

Results: We enrolled 49 men and 55 women, ranging in age from 20-80 years (mean, 52 years). The number of subjects in each group was 18 (group 1), 55 (group 2), 22 (group 3), 9 (group 4). In simple correlation analysis, sural and ulnar SNAPs were inversely correlated with age. However, SUARs were not correlated with age. The sural and ulnar SNAP mean amplitudes of each four groups were significantly different, respectively (sural amplitude: p<0.001, ulnar amplitude: p<0.001). However, mean SUARs of each groups were not significantly different (p=0.296).

Conclusion: Our results suggested that sural and ulnar SNAP amplitudes adjusted for age must be taken into account in the electrodiagnostic studies. Because SUAR is independent of age, that may be helpful in evaluation in polyneuropathy.

Disclosure: Nothing to disclose

EP2218

Peripheral stroke: Case report

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Background and aims: The vasculitis confined to the peripheral nervous system (PNS) rare. Classically this affection is revealed with a multifocal neuropathy, and a brutal onset is uncommon. We describe a case of PNS vasculitis with an acute <<vascular>> onset.

Methods: A 72 years old woman was admitted for weakness evaluation. Few hours before admission, she developed a symmetric numbness and tingling of the limbs. The clinical examination showed a symmetric tetraparesis predominantly in the lower limbs and distally on the upper limbs, she had an absent tendon reflexes at the ankles, a gloves and socks type hypoesthesia, and truncular amyotrophy. The ENMG revealed a symmetric motor and sensitive polyneuropathy with denervation signs. The neuromuscular biopsy revealed a vasculitis of the nerve and muscle samples. All the other secondary causes of vasculitis (neoplastic, toxic, infectious, and systemic) were ruled out after several tests. The diagnosis of primitive vasculitis of the PNS was definite and the patient received steroids and immunosuppressants with a favorable evolution.

Results: We are before an acute <<vascular>> onset of the PNS vasculitis, with a bilateral, symmetric, and synchronized polyneuropathy. In our knowledge, no cases of brutal polyneuropathy revealing a PNS vasculitis were reported. In 30% of the cases, the affection had a distal onset, was both motor and sensitive, and non-symmetric with a tendency of becoming bilateral.

Conclusion: This case illustrates the importance of a meticulous examination and collection of the patient's history in finding the vascular onset of a peripheral neuropathy, and the importance of the biopsy in atypical cases.

Disclosure: Nothing to disclose

EP2219

Pseudotumour cerebri in the Guillain-Barré syndrome

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Background and aims: Pseudotumour cerebri is a rare complication of Guillain-Barre syndrome (GBS), occurring in about 4% of the cases.

Methods: A patient who had the GBS with associated increased intracranial pressure (ICP) and papilledema is described.

Results: A 22-year-old woman was admitted to our department with a two-week history of an upper respiratory tract infection, followed by tingling in the feet and weakness of the lower limbs. On examination, she had moderate proximal weakness of her legs. The limbs were areflexic with flexor plantar responses. Proprioceptive sensation was impaired. Nerve conduction studies showed slowing of velocities and a delay in F waves consistent with the GBS. Lumbar puncture (LP) yielded raised protein in the cerebrospinal fluid (CSF) (3,5 g/L), with a normal cell count. She had motor rehabilitation without recourse to plasma exchange since she was in the plateau phase. Seven weeks after presentation, the patient developed nausea, vomiting and headache. Fundoscopy revealed papilloedema. Brain MRA was normal. LP performed revealed clear CSF with an opening pressure of 36 cm H₂O and no cells, a normal glucose level and a protein of 1.5 g/L. She was treated with a carbonic anhydrase inhibitor and repetitive LPs. Two months later, she was well with no headaches and the papilloedema had resolved.

Conclusion: Pathogenesis of raised ICP remains unclear. Both decreased absorption of CFS and cerebral edema have been suggested. The high concentration of CSF protein may lead to a decreased CSF absorption in arachnoid villi. Treatment remains poorly understood.

Disclosure: Nothing to disclose

EP2220

Questionnaires linked to the Charcot-Marie-Tooth Italian National Registry

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Background and aims: The Charcot-Marie-Tooth disease (CMT) Italian National Registry collects a series of genetic and clinical information.

Methods: Patients adhering to the Registry can also fill online self-reported questionnaires related to five issues: pregnancy; orthotics; skeletal deformity surgery; anesthesia; sleep disorders. By December 2016, 180 patients and 30 healthy controls filled the questionnaires. Data collection is ongoing.

Results: Pregnancy: 46/73 CMT women had at least one pregnancy; complications ranging from mild to severe occurred in 44/108 pregnancies (9/42 in controls). CMT worsened in 7 pregnancies (6 patients) with no recovery in 5 instances. Prenatal diagnosis was performed in 8/108 pregnancies. Satisfaction related to surgical procedures for foot deformities, assessed with VAS (score 0-10), was 6.4 ± 3.5 (n=110). Repeat surgery was required in 9/72 instances. Sleep: the Epworth Sleepiness Scale questionnaire revealed abnormalities of sleep in 44/142 CMT patients (31%) and in 5/30 controls (17%). Pittsburgh Sleep Quality Index (range 0-21, 0 good sleep): most CMT subjects (123/138; mean 9.1 ± 3.2), but also controls (27/30; 8.6 ± 2.9) are not good sleepers. Fatigue: scores of Modified-Fatigue Impact Scale (range 0-82, 0 no fatigue) were higher for CMT (mean 33 ± 18.2) than controls (mean 16.6 ± 12.5). Hospital Scale for Anxiety and Depression: 63/138 CMT subjects had mild-to-severe anxiety and 35/138 mild-to-severe depression as compared to 7/29 and 4/29 controls, respectively. Data analysis on orthotics and anesthesia is ongoing.

Conclusion: The first data analyses confirm that there are problems related to all the five domains explored, that will need to be specifically addressed in patients' care.

Disclosure: Supported by Telethon-UILDM grant GUP13006. On behalf of the Italian CMT Network

EP2221

The importance of correlation between the conduction velocities values in different segments of median nerve and anti-insulin antibodies titer in the serum of patients with diabetes type 1

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Background and aims: For early diagnosis of diabetic neuropathy (DN) different methods with various levels of sensitivity and specificity were used and they were often not satisfactory.

Methods: In 45 patients with diabetes type 1 (DM1) without clinical signs of neuropathy (experimental group- EG) and 45 healthy subjects (control group- CG), we registered motor (MCV) and sensory (SCV) conduction velocity (in m/s) in different segments of median nerve (MN) (on the hand, forearm and upper arm). In the serum of DM1 patients titer of anti-insulin antibodies was determined by Elisa method. Statistical analysis was done by using SPSS software (t-test, Pearson two-tail correlation study).

Results: In EG we registered significant lower MCV NM values in the hand - the middle third of forearm segment compared to CG (44.78 ± 7.83 vs 64.65 ± 6.93 ; $p < 0.05$) and significant lower SCV NM values in the middle third of forearm - distal third upper arm segment in EG versus CG (45.92 ± 9.74 vs 72.37 ± 9.12 ; $p < 0.05$). We registered significant correlation ($p < 0.05$) between MCV NM in the hand - the middle third of forearm segment values and the titer of anti-insulin antibodies.

Conclusion: The determination of MCV NM values in the hand - the middle third of forearm segment at diabetics type 1 without clinical signs of neuropathy is fast and simple method for early diagnosis of DN. Besides, titer of anti-insulin antibodies has some role in complex pathogenesis of DN at DM1 patients.

Disclosure: Nothing to disclose

EP2222

Cancelled

EP2223

Features of pain in chronic inflammatory demyelinating polyneuropathy (CIDP)M. Sialitski¹, V. Ponomarev²*¹Belarusian Medical Academy of Postgraduate Education, Minsk, Belarus, ²Head of Department of Neurology and Neurosurgery of BelMAPGE, Belarusian Medical Academy of Postgraduate Education, Minsk, Belarus*

Background and aims: Pain is the most common symptom of a variety of pathological conditions, including autoimmune diseases of the nervous system. It has a different character and intensity. CIDP is one of the most common forms of autoimmune disease.

Methods: Main group in our study consisted of 59 patients diagnosed with CIDP (mean age: 58.2±17.2 years) based on neurological examination and EMG that meets international criteria for diagnosis of CIDP (INCAT, 2001). Disease duration ranged from 6 months to 11 years. Pain was assessed quantitatively using of Visual Analog Scale (VAS) and qualitatively using of Leeds Assessment of Neuropathic Symptoms and Signs Pain Scale (LANSS).

Results: Pain as a the symptom of CIDP was found in 42 patients (71.2%) according to VAS. Neuropathic pain in these patients was found in 9 patients (15.3%) according LANSS. The median level of VAS was 6.16 [4.38; 7.35]. Correlations were found between the duration of disease and the degree of pain ($R=-0.32$, $p=0.042$), as well as between the degree of pain and the degree of paresis ($R=-0.46$, $p=0.029$). Thus, our results demonstrate that pain is less acute in cases with longer history of CIDP and in cases when paresis is more severe.

Conclusion: Neuropathic pain meets only in 21.43% of patients with pain symptom in CIDP.

The reduction of pain might be associated with degeneration of peripheral nerve during the progression of the disease, as suggested by the EMG results.

Disclosure: Nothing to disclose

EP2224

Microcirculatory and thermoregulatory dysfunctions in diabetic polyneuropathyZ. Stoyneva, S. Dermendjiev²*¹Department of Neurology, Sofia and Plovdiv Medical Universities, University Hospital St. Ivan Rilsky, Sofia, Bulgaria, ²Department of Occupational Diseases, Plovdiv Medical University, Plovdiv, Bulgaria*

Background: Diabetes mellitus (DM) is an increasing global epidemic, type 2 diabetes (T2DM) comprises the majority of diabetics, and associated diabetic polyneuropathy (DPN) is its most common and disabling complication. Microcirculatory dysfunctions in DM are of pivotal importance for the development of diabetic complications.

Aim: to evaluate microcirculatory and thermoregulatory disorders in patients with T2DM and DPN.

Methods: Fifty five T2DM subjects met the case definition for DPN and were included into research together with 46 sex and age matched healthy controls. The nutritious skin vessels were investigated by nailfold videocapillaroscopy and the big tiptoe skin blood flow was measured at baseline and during axon-mediated reactive hyperemia responses to cutaneous heating (44 degrees Celsius) followed by relative cooling to 32 degrees Celsius by laser Doppler flowmetry (LDF).

Results: Reduced capillary density and spastic capillaries were found in the prevailing part of the patients (89%) while the baseline LDF perfusions were higher in T2DM. The heat- and cold-induced perfusion responses were attenuated, the hyperemic peak was significantly reduced in the patients compared with the controls. The vasodilator heat-induced perfusion indices were lower and the vasoconstrictor perfusion indices during relative cooling were higher in DPN patients in relation to healthy subjects ($p<0.0001$).

Conclusion: The combination of T2DM and polyneuropathy is associated with a decreased number of nutritious skin vessels and capillary spasm, an increased thermoregulatory skin blood flow at rest and reduced axon-reflex mediated heat-induced cutaneous vasodilation in the feet.

Disclosure: Nothing to disclose

EP2225

Diagnostic validity of sympathetic skin response in small-fibre neuropathy

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Background and aims: Sympathetic skin response (SSR) is a simple and widely available test of sudomotor functions. The afferent part of this polysynaptic reflex is variable, while small unmyelinated C-fibres comprise the efferent part of its arch. The aim of the study was to evaluate the diagnostic validity of SSR in patients with sensory small-fibre neuropathy.

Methods: SSR was recorded from the palms and soles of 69 patients with painful sensory neuropathy (33 of them with pure SFN and 36 with mixed small and large nerve-fibre dysfunction) using electrical stimulation and inspiratory gasp stimuli. Small nerve-fibre affection had been confirmed by reduced intraepidermal nerve-fibre densities (IENFD) in skin biopsy samples in all cases. Further, 89 healthy controls were examined and age-stratified normal limits for amplitudes, latencies and reproducibility of response were established based on the results.

Results: The latencies of SSRs and their amplitudes were of very low diagnostic validity in sensory neuropathy patients. In fact, the absence of an SSR response proved the most reliable abnormality. However, using just this parameter, dysfunction of small autonomic nerve-fibres was disclosed in only in a small proportion of our sensory neuropathy patients: its sensitivity did not exceed 10% in pure SFN patients or 33% in those with mixed small and large nerve-fibre dysfunction (where more pronounced small sensory nerve-fibre affection had already been established in terms of IENFD values).

Conclusion: In view of its demonstrably low sensitivity, SSR should not be used as the only test when seeking to confirm sensory small-fibre neuropathy.

Disclosure: Nothing to disclose

EP2226

Crohn's disease and polyneuropathy

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Background and aims: Aim of the present study was to establish the clinical, electrophysiological and pathological features of neuropathy in patients with Crohn's disease (CD).

Methods: Biopsy specimens were obtained from over 700 sural nerves biopsies. The selection of patients was done according to the criteria for the diagnosis of CD. Complete laboratory, clinical electrophysiological and pathological studies were performed in all cases.

Results: We found nerve biopsies of 4 patients with neuropathy and CD. The pattern of neuropathy was distal symmetrical sensorimotor polyneuropathy, while the pathological findings showed demyelination with predominant axonal degeneration and a varying pattern of myelinated fiber loss with no vasculitic changes.

Conclusion: There is association of polyneuropathy and CD and it is important to recognize it in the early stage because remission depends on immunosuppressive therapy.

Disclosure: Nothing to disclose

EP2227

Thoracic outlet syndrome - amyotrophic form: Clinical and electrophysiological presentation of 9 cases

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Background and aims: Thoracic outlet syndrome (TOS) is a more unknown and rare entity, of polymorphous and misleading clinical presentation. A Meticulously electrophysiological study involving the study of the internal cutaneous brachial nerve (C8-D1) is essential.

We report the clinical and etiological aspects of the (TOS) in its amyotrophic form; underline the interest of the study of the internal brachial nerve brains (BCI).

Methods: Prospective analysis of the clinical, electrophysiological and etiological aspects of nine observations of (TOS) for 7 women and 2 men, aged from 18 to 61 with an average age of 41 years.

Results: The paresthesias of the hand and the forearm with heaviness and amyotrophy of the hand were noted in all our patients. At the Electromyogram (EMG) there was a decrease in the amplitudes of the motor potentials of the median and ulnar nerves. The sensory potentials of the median nerve were normal, those of the ulnar nerve decreased and there was an alteration of the sensory potential of the BCI. In 3 patients an apophysomegaly, 5 cervical ribs and 1 patient associating the two anomalies. At angioscanner an aberrant subclavian artery (1 case). There will be a discrete improvement post-surgery.

Conclusion: The syndrome of the DCTB is difficult to diagnose based on clinical arguments confronted by a meticulous ENMG study especially before the amyotrophic forms.

Disclosure: Nothing to disclose

EP2228

Clinical characteristics of patients with chronic axonal neuropathy with and without gluten sensitivity

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Background and aims: After cerebellar ataxia, peripheral neuropathy (PN) is the second commonest neurological manifestation of gluten sensitivity. We compared the clinical characteristics between PN patients with and without gluten sensitivity (GS).

Methods: Between January 2016 and December 2016 all consecutive patients attending a specialist clinic that focuses on gluten and idiopathic neuropathies, were invited to participate. All patients were examined clinically and neurophysiologically. Pain was assessed via the DN4 questionnaire and the visual analogue scale (VAS). Overall Neuropathy Limitations Scale (ONLS) was used to assess the severity of neuropathy.

Results: Of the 102 PN patients recruited, 76 (74.5%) had sensorimotor axonal neuropathy, 25 (24.5%) had sensory ganglionopathy and 1 (1.0%) had mononeuritis multiplex. Fifty-one patients (50%) had GS (positive serological markers for GS). Fifteen patients (14.7%) reported pain as the first symptom of their neuropathy. Prevalence of pain was 60.8%. The two groups did not differ significantly regarding age, gender, presence of pain, type and severity of neuropathy. Patients with GS reported less intense pain (VAS 6.8±2.3 versus 8.3±1.0, p<0.01). Total DN4 scores did not differ between the two groups. Patients with GS reported numbness whereas patients without GS reported tingling to be the commonest neuropathic feature accompanying their pain.

Conclusion: Although pain is similarly prevalent between patients with gluten neuropathy and those with idiopathic neuropathy, gluten neuropathy appears to be a less painful.

Disclosure: Nothing to disclose

Sleep disorders 2

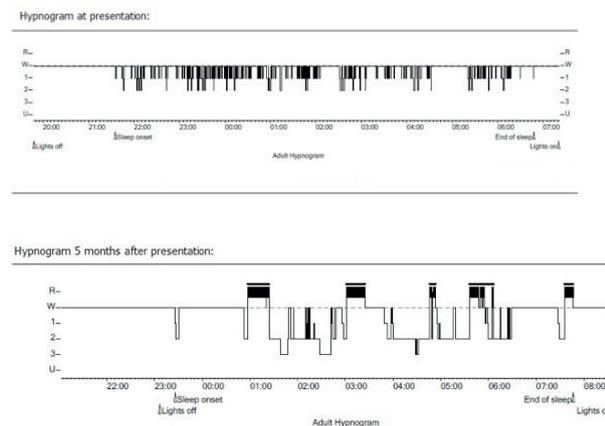
EP2229

Evolution of sleep abnormalities in a patient with anti-Lgi1 antibody associated autoimmune encephalitis.

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Background: A 53-year-old man was referred to us for late-onset epilepsy with recurrent generalized tonic-clonic seizures. By the time of referral, he also complained of restless sleep with continuous irregular limb movements, vivid dreams, hypersomnolence, hyperhydrosis, mild progressive cognitive decline and increased emotionality. He experienced episodes with altered taste and smell and/or bilateral piloerection, and episodes with sudden motor unrest (often rising from prone/sitting position), staring, orofacial automatisms and/or confusion during 1-5 seconds. Symptoms first appeared 2 months prior to referral, shortly after resection of a melanoma (pT1a).

Methods: Neurological examination showed multifocal myoclonus, but was otherwise normal. Brain imaging was unremarkable. CSF analysis showed mildly elevated protein. Antibody testing in plasma and CSF was positive for anti-leucine-rich glioma-inactivated 1 (Lgi1) but not for anti-Caspr2 antibodies. Continuous EEG during episodes with smell/taste sensations did not show epileptiform abnormalities. EMG confirmed the presence of myoclonus, but showed no signs of neuromyotonia. Neuropsychological evaluation showed frontal involvement (attention deficits, slowed information processing speed). Polysomnography showed severe sleep fragmentation and absence of deep NREM and REM-sleep. Screening for malignancy was negative. Treatment with corticosteroids, plasmapheresis and azathioprine resulted in resolution of symptoms. On follow-up polysomnography, sleep fragmentation was resolved but sleep architecture remained disturbed with a sudden onset REM period and decreased amount of deep sleep.



Conclusion: We describe a case of anti-Lgi1 antibody associated autoimmune encephalitis, with symptoms closely resembling Morvan's syndrome, but without myotonia. Treatment response in autoimmune encephalitis is variable, and signs and symptoms may persist or recur.

Disclosure: Nothing to disclose

EP2230

Cancelled

EP2231

Correlation between parameters of autonomic nervous system function and overnight polysomnography in patients with sleep disorders

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Background and aims: Previous studies suggest that patients with sleep disorders have higher risk of autonomic nervous system (ANS) dysfunction. The aim of this study was to correlate ANS parameters with overnight polysomnography (PSG) features.

Methods: In this cross-sectional study 47 consecutive patients (25 men, mean age 48.23±16.09 years) who underwent overnight polysomnography were recruited (19 patients with obstructive sleep apnea syndrome (OSAS), 28 non-OSAS subjects). They all underwent PSG and standardized battery of ANS testing, including blood pressure and heart rate response to Valsalva maneuver, deep breathing test and head up tilt table test. Adrenergic and cardiovagal scores of the Composite Autonomic Scoring Scale (CASS) were determined.

Results: RESULTS: Out of 47 subjects, interpretation of both cardiovagal and adrenergic CASS score was available for 40 subjects, 42.5% had CASS cardiovagal score ≥ 1 , 52.5% had CASS adrenergic score ≥ 1 . Negative correlation was found between CASS cardiovagal score and total sleep time ($r_s = -0.368$, $p = 0.020$). Positive correlation was found between CASS cardiovagal score and sleep latency ($r_s = 0.445$, $p = 0.004$). Oxygen saturation was found to have a negative correlation with CASS cardiovagal score ($r_s = -0.379$, $p = 0.027$). Positive correlation was found between CASS cardiovagal score and desaturation index per hour ($r_s = 0.393$, $p = 0.022$). CASS adrenergic score did not show significant correlation with any PSG parameters.

Conclusion: CONCLUSION: The results of this study are suggesting that parasympathetic nervous system dysfunction is associated with impaired sleep structure (sleep latency and total sleep time) and oxygen saturation.

Disclosure: Nothing to disclose

EP2232

Cancelled

EP2233

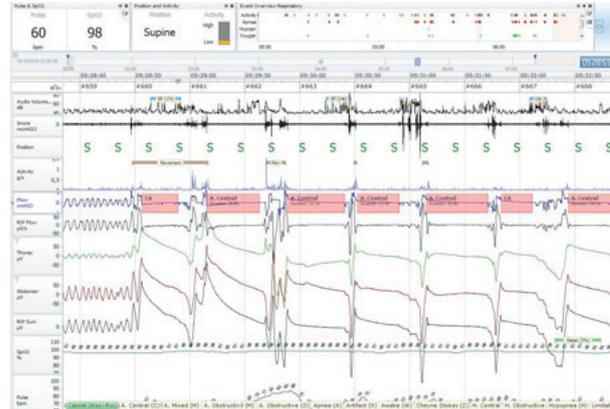
Catathrenia, a rare sleep disorder- Clinical experience, diagnosis and treatment at sleep unit

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Background and aims: Catathrenia is a rare sleep disorder that affects young adults characterised by expiratory groaning during sleep, preceded by a deep inspiration which occurs specially during REM phases. Since its original description, there have been few cases reported. Patients are normally unaware but typically bed partners are troubled, often deriving in social problems. Continuous positive airway pressure (CPAP) and surgery have been proposed as treatment. Mandibular advancement devices (MADs) have never been used before.

Methods: We studied the clinical course, polysomnogram (PSG), spirometric findings and outcomes after the treatment of eight patients with a diagnosis of catathrenia at our center.

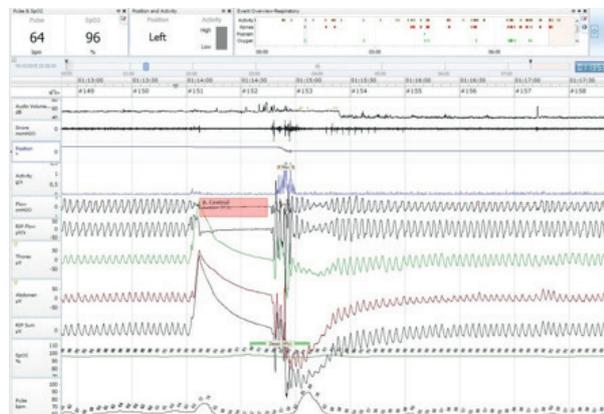
Results: We included eight patients (5 men, 3 women) with a mean age at diagnosis of 28.6±4.9 years (range 22–38 years). The chief complaint was noises during sleep (62,5%), disturbances to bed partner (25%) and bad sleep quality (50%). All the patients referred that it was a nightly problem. The number of catathrenia events (single or cluster) during overnight PSG varied between 8 and 24 per patient (mean 14.8). Their exhalation and sound duration range was 23s - 423 s. CPAP treatment was proposed for two of the patients. One patient had Obstructive Sleep Apnea (OSA), showing an improvement in his sleep quality. The other patient had significantly fewer events of groaning with CPAP and improved her sleep quality. We proposed treatment with a MAD to one patient, without improvement.



Catathrenia's cluster.

Conclusion: Catathrenia patients may benefit from CPAP, specially those with coexistence of OSA. In our experience, MAD was not an effective treatment.

Disclosure: Nothing to disclose



Catathrenia single

EP2234

Sleep disturbance and the risk for cognitive decline: Assessment of visual attention components in patients with insomnia

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Background and aims: Chronic primary insomnia (CPI) is a highly prevalent sleep disorder in subjects >50 years of age and related to psychological distress. As both sleep deprivation and increased stress susceptibility have been shown to represent risk factors for neurodegeneration, CPI patients may be subject to a higher probability for developing progressive cognitive impairment. In fact, in patients with CPI, lower sleep quality has been found to be associated with hippocampal atrophy and cognitive decline. Similar brain and cognitive changes prevail in patients with mild cognitive impairment (MCI), who bear an increased risk for developing dementia. Our own previous work in MCI patients, applying the conceptual framework of the 'theory of visual attention' (TVA), has identified an elevated perceptual threshold in comparison to age-matched healthy participants in a whole report task.

Methods: In the present study we assessed a sample of 16 CPI patients and sex matched controls with TVA-based whole report to test the hypothesis that CPI patients also show a significant increase of the perceptual threshold.

Results: Compared to a healthy control group, we found no significant differences with respect to TVA-based parameters of processing capacity. However, within the patient group, the perceptual threshold values were significantly related to the subjective evaluation of insomnia severity (ISI questionnaire). Also, higher threshold values in CPI patients were significantly correlated to polysomnography indices, i.e. sleep efficiency index, and arousal index.

Conclusion: TVA-based assessment of visual processing capacity may be able to identify CPI patients with an increased risk for cognitive decline.

Disclosure: Nothing to disclose

EP2235

Narcolepsy with cataplexy in a patient with anti-Hu antibodies

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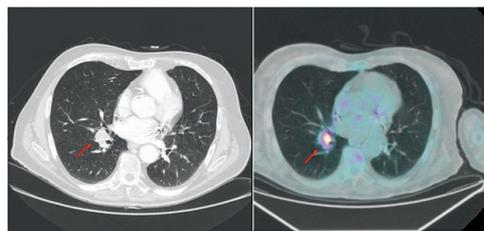
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Background and aims: Type 1 narcolepsy (NT1) is a central hypersomnia due to the loss of hypocretin-producing

neurons of a likely autoimmune etiology. 'Symptomatic' forms have been rarely described.

Methods: A 85-year-old male, heavy smoker and with many cardiovascular risks factors, was admitted because of a six-months history of subacute onset of behavioral change, excessive daytime sleepiness, generalized weakness, and episodes of loss of muscle tone in the limbs and slurred speech, triggered by emotions. Neurological examination revealed subcontinuous fluctuations in muscle tone with ptosis, facial grimaces, muscle sagging of upper limbs and generalized hypotonia. Polysomnography and multiple sleep latency test documented, respectively, disrupted nocturnal sleep with REM sleep behavior disorder and 5/5 sleep-onset REM sleep periods with pathologically sleep latency. Polygraphic recordings documented cataplectic status. HLA typing was negative for HLA-DR15-DQB1*0602 antigens. Paraneoplastic screening disclosed a serum positivity of anti-neuronal nuclear antibody, type 1 (anti Hu), while the analysis of the cerebrospinal fluid revealed decreased hypocretin-1 level (146,83 pg/mL). Total CT scans finally showed a hilar-perihilar lesion in the right lung that displayed hyperfixation at the whole-body fluorodeoxyglucose positron emission tomography (PET).



Chest CT scan with hilar-perihilar lesion in the right lung; 18F-FDG PET with hyperfixation of nodular formation

Results: A diagnosis of symptomatic narcolepsy with cataplexy in presence of anti-Hu antibodies and lung cancer was made. A symptomatic treatment with modafinil, sodium oxybate and venlafaxine was started, with only partial clinical benefit.

Conclusion: This is the first report of symptomatic narcolepsy with cataplexy in patient with positivity of anti-Hu antibodies. Atypical age, subacute onset and cataplexy severity point to a the secondary nature of the symptoms.

Disclosure: Nothing to disclose

EP2236

Cancelled

Monday, 26 June 2017

Cerebrovascular diseases 6

EP3001

The role of BNIP3 in acute cardiac injury following ischemic stroke

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Background and aims: Cardiac diseases are common post-stroke and are associated with increased morbidity and mortality. One possible mechanism of acute cardiac injury is the neurogenic myocardial damage, where the cerebral injury is disturbing the normal sympathetic and parasympathetic neuronal outflow to the heart leading to cardiac damage including myocardial infarctions. A consequence of an increased sympathetic activity is an exaggerated norepinephrine efflux from cardiac sympathetic nerve terminals into the myocardial interstitium with prolonged opening of the β_1 -adrenergic receptor-controlled calcium channels. Abnormal intracellular Ca^{2+} -handling, leads to mitochondrial dysfunction, presumably mediated by the pro cell death protein BNIP3, and generation of reactive oxygen species (ROS). The exact mechanism is not completely understood and the major objective of this project is to characterize the molecular phenotype of the neurogenic myocardial damage post-stroke.

Methods: Our data demonstrate acute myocardial damage in wild-type mice after right-sided transient middle cerebral artery occlusion (tMCAO).

Results: Notably, the size of myocardial damage correlated with the brain infarct volume and triggered a ~4-fold elevation of troponin t levels that were detectable 20 h after stroke. Similar effects were found using the β_1 -adrenergic receptor stimulator isoproterenol, an established model of heart failure. Following either cerebral stroke or isoproterenol treatment, higher levels of BNIP3, cardiac troponin t, ANP, BNP and norepinephrine were found in blood and heart samples at distinct time points.

Conclusion: We found expression of the pro cell death protein BNIP3 in the heart after cerebral ischemia and we will further investigate the role of BNIP3 in mediating neurogenic cardiac damage.

Disclosure: Nothing to disclose

EP3002

A study of clinical features, risk factors and short-term outcome of ischemic stroke in patients with and without atrial fibrillation in a North African population

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Background and aims: There is poor data concerning clinical profile and prognosis of ischemic stroke (IS) in patients with atrial fibrillation (AF) from North Africa. We attempted to estimate characteristics in demographic and clinical features, risk factors and short-term outcome of IS patients with and without AF from Tunisian population.

Methods: A prospective study was conducted from February to May 2015 at Habib Bourguiba Hospital (Sfax, Tunisia) including all first acute stroke patients (≥ 18 years). Patients with AF (group 1) and without AF (group 2) were analyzed for demographic characteristics, stroke risk factors, clinical characteristics, location of infarct and prognosis.

Results: Two hundred patients were enrolled. Out of 200, 152 had IS. Forty-nine (32.23%) patients had AF (non-valvular AF: 93.78%). There were significant differences seen in age (group1: 73.61 \pm 14.22 years versus group 2: 67.03 \pm 13.94 years; $p=0.008$) and gender (group 1: men 48.98%/ women 51.02% versus group 2 men 67%/women 33%; $p=0.03$). Risk factors such as diabetes (18.36% versus 42.71%, $p=0.03$) and active smoking (32.65% versus 49.51%, $p=0.05$) were less prevalent in patients with AF. The mean of initial NIHSS was significant (group 1:12.67 vs group 2: 8.60; $p=0.003$). Extensive middle cerebral artery infarction were more significant in group 1 (26.53% vs 10.37%). Patients with AF had poor outcome at one month (mean Functional Independence Measure score: 75.29 vs 92.13; $p=0.029$).

Conclusion: In our population, the frequency of non-valvular AF is quite high. These patients had less risk factors but poor outcome at one month.

Disclosure: Nothing to disclose

EP3003

Early and late epileptic seizures after stroke

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Background and aims: Epileptic seizures are common complication after stroke, divided into early seizures, which occur in the first fourteen days, and late ones which occur more than fourteen days after stroke. The aim of the research is to determine the relationship between the early and late seizures, and the influence of comorbidity on seizures.

Methods: The research is retrospective and includes patients with poststroke seizures who were hospitalized at the Clinic of Neurology in Novi Sad, in the period from 2013. to 2016. year.

Results: The research included 54 patients with poststroke seizures, half were male, half female, mean age 64,4±4,5 years. 36 (67%) patients had ischemic, and 18 (33%) patients had hemorrhagic stroke. Generalized seizures had 36 (67%) patients, focal seizures had 18 (33%) patients, while 2 patients had status epilepticus. In the group of patients with ischemic stroke late seizures were more common, while in the group of patients with intracranial hemorrhage early seizures were more often, which was statistically significant ($p=0.04$). Patients with cardioembolic stroke were more likely to have generalized seizures ($p=0.048$). Early attacks were more often registered in patients suffering from anemia and in group of smokers.

Conclusion: Age, gender, size and localization of morphological lesions do not significantly affect the type of seizures after stroke. Intracranial hemorrhage is often followed by early seizure, while ischemic stroke is accompanied by late seizures. Generalized seizures are more common in patients with cardioembolic stroke. Early attacks usually occur on first day after stroke.

Disclosure: Nothing to disclose

EP3004

Right hemisphere ischemic stroke in a 24-year-old patient with antithrombin III deficiency presenting as severe oral apraxia and anarthria

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Background and aims: Antithrombin III (ATIII) is a protease that inhibits coagulation by neutralizing thrombin activity. ATIII deficiency is a rare condition and an uncommon cause of stroke.

Methods: Case report

Results: A 24-year-old left-handed woman was admitted to the neurology department due to a sudden onset of speech impairment and mild weakness of her left arm. She had been on Acenocoumarol treatment for 6 years due to recurrent episodes of deep venous thrombosis. The anticoagulant medication was discontinued 10 days prior to the stroke. Her neurological examination revealed mild left central facial and left arm weakness and anarthria with normal comprehension and writing. Oral apraxia was present and the patient was unable to follow the instructions to protrude her tongue, whistle or puff out her cheeks. Spontaneous movements of the tongue, lips and jaw were intact. The patient was also unable to voluntarily swallow saliva. However, pharyngeal and esophageal phases of swallowing were preserved. Limb apraxia was absent. Magnetic resonance imaging of the brain showed a right insular cortex and frontal operculum infarction. The patient's ATIII activity was decreased in two independent measurements (39.7% and 31%), while protein S (75.4%), protein C (113%), APC-R (2.31) and LAC (1.2) showed normal values. Limb weakness, speech, swallowing and oral praxia gradually recovered during the following weeks. The patient was treated with low molecular weight heparin, followed by Warfarin. Genetic testing is ongoing.

Conclusion: The incidence of thrombotic events, including stroke, is increased in ATIII deficient patients. This condition requires treatment with anticoagulant medication.

Disclosure: Nothing to disclose

EP3005

Cancelled

EP3006

The studying of shear stress in the development of endothelium dysfunction in patients with spondylogenic vertebrobasilar insufficiency

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Background and aims: A shear stress is known as a force applied to the upper layer of the laminar-flowing liquid that causes displacement of the underlying layers in relation to each other in direction of the applied force. The stream of blood deforms endothelial membrane, which leads to a wide range of regulatory influences.

The aim was to study the role of shear stress in the development of endothelium dysfunction (ED) in patients with spondylogenic vertebrobasilar insufficiency (SVBI).

Methods: For an assessment of nature of shear stress in vessels of vertebrobasilar system Stewart's index (ISD) was studied. Concentration of endothelin-1 (ET-1) in serum of blood by immunoenzymatic analysis was evaluated.

Results: In group of 98 patients with SVBI the rise of concentration of ET-1 in blood serum (2.84 ± 0.09 femtomol/ml against 1.25 ± 0.08 femtomol/ml) was found, against the S-NO level recession (0.18 ± 0.07 microns/l against 0.45 ± 0.02 microns/l) that demonstrated vasopressin tendency of the endothelial vasoregulation. The assessment of ISD revealed rising of it concerning left VA on $31.6 \pm 0.69\%$ from control, right VA of $20.7 \pm 0.64\%$, BA of $15.6 \pm 0.37\%$ ($p < 0.05$), indicating shear stress in the vertebrobasilar vessels in comparison with control.

Conclusion: The carried-out correlation analysis confirmed the interrelation of a condition of shear stress on the basis of the assessment of a ISD and ED of patients with SVBI, revealing positive correlation dependence between the ISD in BA and ET-1 level ($r = +0.41$); negative correlation dependence between S-NO and ISD in BA ($r = -0.22$) ($p < 0.05$).

Disclosure: Nothing to disclose

EP3007

Obstructive sleep apnea in stroke patients

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Background and aims: Ischemic stroke is one of the most sociologically important diseases and its linking with obstructive sleep apnea has been discussed throughout the recent years. Most of the data has come from many summary, cross, meta analyses which have shown a definite link between the two conditions. We present a localised study on acute stroke patients with obstructive sleep apnea (OSA), its treatment with CPAP or BPAP, and clinical outcome and follow up.

Methods: Detailed patient history, including socio-demographics; somatic and neurological status; assessment of concomitant diseases and treatment; stroke severity; OSA severity assessment; respiratory poligraphy and/or polisomnography; CPAP/BPAP treatment, patient follow up.

Results: 30 patients have been fully analysed including follow up. They were divided into several common groups - patients that started CPAP/BPAP treatment during hospital stay, patients starting treatment after hospital discharge, patients without therapy, patients with treatment only in the acute phase. All but one of the patients had newly diagnosed stroke and sleep apnea. 2 patients required BPAP therapy while all others had CPAP therapy initiated. We found a close relation to sleep apnea and stroke severity - those with a higher NIHSS score had severe OSA (marked by a high AHI) in most cases. Patients undergoing OSA treatment show a better clinical outcome on follow up but time of treatment initiation didn't show any influence on outcome.

Conclusion: Sleep apnea is a known risk factor for the development of stroke, but also a known consequence. Treatment of OSA following stroke shows a significant profit for clinical outcome.

Disclosure: Nothing to disclose

EP3008

Intravenous thrombolysis in minor ischaemic stroke – do the octogenarians worse?

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Background and aims: Minor ischaemic stroke (MIS) is not unanimously defined yet. Benefit of Intravenous thrombolysis (IVT) in MIS is not clear in general. Benefit of IVT in MIS in the elderly, is matter of discussion.

Aim of the study: Safety and benefit of IVT in patients over 80 years comparing to younger ones.

Methods: Prospectively and consecutively enrolled cohort in period 1/2014 to 9/2016. Inclusion criteria: MIS (defined as NIHSS 0-4), onset \leq 4,5h or unknown, prestroke performance modified Rankin scale (mRS) 0-2. Exclusion criteria: haemorrhagic stroke. Cohort was split into two groups: „elderly“ (means \geq 80 years old) and „<80“. Outcome: 3 month after stroke per mRS; symptomatic intracranial haemorrhage (sICH).

Results: Cohort comprised 177 patients. Group “elderly”: 30 patients, 13 males (43.3%), mean age 84.0 ± 3.15 years; OTT: 130.1 ± 46.9 , unknown onset: 3 (10.0%), DNT 36.9 ± 21.0 . Group “<80”: 147 patients, 84 males (54.7%), mean age 65.9 ± 9.8 years; OTT: 131.5 ± 63.7 , unknown onset: 19 (12.8%), DNT 40.2 ± 20.1 . Admission status and clinical outcome see tables 1-2. Excellent clinical outcome (mRS 0-1) in “elderly” and “<80” were 66.7% and 76.5% respectively, and sICH: 1 (3.3%) and 2 (1.3%) respectively.

NIHSS	Admission clinical finding			
	elderly		< 80	
0	1	3,3%	10	6,8%
1	2	6,7%	13	8,8%
2	9	30,0%	34	23,1%
3	9	30,0%	44	29,9%
4	9	30,0%	46	31,3%
total	30	100,0%	147	100,0%

Table 1: Admission NIHSS

mRS	3 month clinical outcome			
	elderly		< 80	
0	14	46,7%	96	65,3%
1	6	20,0%	18	12,2%
2	4	13,3%	16	10,9%
3-5	4	13,3%	13	8,8%
6	2	6,7%	4	2,7%
total	30	100,0%	147	100,0%

Table-2: 3month outcome (mRS)

Conclusion: IVT of MIS in the elderly is slightly worse than in the younger, but still highly beneficial and safe. Bleeding complications remain low.

Age should not be the exclusion for IVT neither in general nor in MIS.

Disclosure: Nothing to disclose

EP3009

Safety of acupuncture for patients taking warfarin or antiplatelet medications

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Background and aims: Anticoagulant and antiplatelet therapy are widely used as preventive measures and treatment for cardiovascular and cerebrovascular diseases. Bleeding is a significant complication of anticoagulant and antiplatelet medications. With the growing use of acupuncture and the potential concomitant use of such medications, studies on the safety of acupuncture are necessary. The objective of this study was to evaluate the safety of acupuncture for patients taking warfarin or antiplatelet medications by comparing the rate of side effects for patients who did not take either of these medications.

Methods: The medical records were searched to identify patients who had received acupuncture treatments at Stroke and Neurological Disorders Center, Kyung Hee University Hospital at Gangdong. Prescribed medications were identified from medical records and each patient was allocated to one of three groups based on the medication they were taking. Group A were taking warfarin, group B were taking antiplatelet medications but not warfarin, group C took neither warfarin nor antiplatelet medications and acted as a control group. Potential side effects that could be attributed to of acupuncture were identified.

Results: A total of 242 patients and 4891 acupuncture treatments were identified. No patients experienced serious adverse events such as extensive bleeding. The occurrence rate of microbleeding (bleeding which stopped within 30 s) was 4.8% for group A, 0.9% for group B and 3.0% for group C.

Conclusion: Acupuncture treatment appears safe even for patients taking warfarin or antiplatelet medications. Large-scale, well-designed studies are needed to confirm these results.

Disclosure: Nothing to disclose

EP3010

Bilateral carotid agenesisN. Pelaez¹, D. Dunlop²¹Cordoba, Spain, ²Radiology, Hospital universitario Reina Sofía, CORDOBA, Spain

Background and aims: Agenesis of the internal carotid artery (ICA) (uni o bilateral) is a rare congenital anomaly, occurring in less than 0.01% of the population. The term absence has been chosen to encompass agenesis, aplasia and hypoplasia of the ICA. Agenesis is use when both, the artery and the carotid canal are absent. It may be asymptomatic or produce symptoms due to vascular insufficiency.

Methods: A 57-year-old female with a history of long-standing bilateral sensorineural hearing loss, hyper gonadotropic hypogonadism and hypothyroidism presented during the last month non-progressive blurry vision and headache. The neuro-ophthalmological examination was normal.

Results: MRI was performed, showing no brain, brainstem or cerebellar findings.

The MR angiogram revealed bilateral agenesis of the ICA with supply to the anterior circulation via carotid-vertebrobasilar anastomoses, accomplished through hypertrophy of the PCOM (posterior communication). The absence of both carotid canals on a skull base CT scan confirmed the bilateral carotid agenesis.

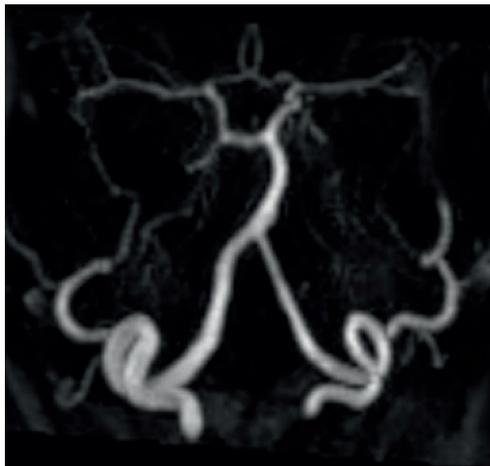


Fig. 1. Coronal time-of-flight MR angiography showing a posterior view of the circle of Willis. There is an enlarged basilar artery and posterior communicating arteries supplying both anterior and medial cerebral arteries. Neither internal carotid arteries are seen.

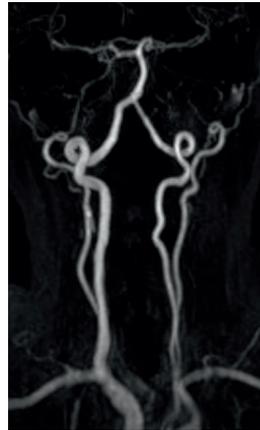


Fig. 2. Coronal time-of-flight MR angiography showing an anterior view of supraortic vessels. There is an absence of both internal carotid arteries, and an enlarged right vertebral artery.



Fig. 3. Axial bone window CT showing the absence of both carotid canals.

Conclusion: The diagnosis of this anomaly has an important implication in thromboembolic disease, and in the surveillance and detection of associated cerebral aneurysms (approximately 35%).

Associations with congenital malformations in different organs have been described, like anomalies in the hypothalamic – pituitary axis and PHACE syndrome.

The cerebral angiography, MR angiogram and the CT scan and are powerful diagnostic tools in these patients, and also in their follow up.

Disclosure: Nothing to disclose

EP3011

Cancelled

EP3012

Cancelled

Cerebrovascular diseases 7

EP3013

An atypical clinical presentation of diffuse cerebral arteriovenous malformation: Diagnostic dilemma between diffuse AVM and cerebral proliferative angiopathy

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Background and aims: Here we present a 37-year-old male patient who was evaluated at our medical center with headache, right-sided weakness and aphasia that was progressively developed within one week. His past medical history was unremarkable and laboratory test results were found to be in normal limits. Cranial MRI (magnetic resonance imaging) revealed diffuse arteriovenous malformation (AVM) that was confirmed with Cerebral DSA (digital subtraction angiography) showing diffuse AVM with nidus. Following Perfusion-weighted MRI revealed hyperperfusion in the entire left hemispheric area. Based on the short time of unresponsiveness symptom of the patient we aimed to evaluate long-term EEG monitoring that revealed electrographic seizure activity on the left centrotemporal region. We have initiated anti-epileptic treatment that led to improvement in his epileptic symptoms while his right-sided weakness and word finding difficulty symptoms remained stable over three months.

Methods: This is an interesting case with subacutely developed clinical findings and prominent cerebral ischemic areas in MRI that are associated with variable cerebral perfusion abnormalities in MRI-Perfusion imaging which finally resembles also a possible cerebral proliferative angiopathy (CPA).

Results: The natural course of CPA has been reported to be less aggressive than the classical clinical progress of the brain AVMalformations. Furthermore, CPA differs from other arteriovenous malformations in their angiomorphology, histology, pathophysiology, epidemiology, natural history, and clinical presentation. However, despite these differences it can be in some atypical cases difficult to differentiate diffuse AVM from CPA.

Conclusion: Here, we present an atypical clinical presentation of radiologically confirmed AVM that is simulating the clinical symptoms of CPA.

Disclosure: Nothing to disclose

EP3014

Tenecteplase in wake-up ischaemic stroke trial

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Background and aims: Patients with wake-up stroke have traditionally been considered ineligible for intravenous thrombolytic treatment. Tenecteplase has pharmacological advantages over alteplase, and can be given as a bolus. We are doing a pragmatic, CT-based, randomised-controlled, open trial of tenecteplase for patients with wake-up stroke; the Tenecteplase in Wake-up Ischaemic Stroke Trial (TWIST).

Methods: Patients with wake-up stroke <4.5 hours and without evidence of large infarct or proximal artery occlusion will be randomised to tenecteplase 0.25 mg/kg plus standard care or standard care alone. Plain brain CT and CT angiography will be done before randomisation and repeated on day 2. CT perfusion will be done at selected centres. Follow-up will be done at discharge (or day 7) and by telephone at 3 months.

The primary effect variable is functional outcome at 3 months, measured by the modified Rankin Scale.

Results: The target is to include 500 patients from centres in Norway, Sweden, Denmark, Finland, Estonia, Lithuania, UK, Ireland and Switzerland. Start of patient inclusion: January 2017. Planned study period: two years. Study questions to be answered:

1. Can thrombolytic treatment with tenecteplase within 4.5 hours of wake-up improve functional outcome at 3 months?
2. Can findings on CT angiography or CT perfusion identify patients who benefit from such treatment, compared to patients without such findings?

Conclusion: TWIST will show whether patients with wake-

up stroke benefit from treatment with tenecteplase within 4.5 hours of awakening, and whether multi-modal CT can be used for selection of patients.

Disclosure: Nothing to disclose

EP3015

Hematoma evacuation or decompressive craniectomy: 11 years of experience in surgical treatment of patients with supratentorial intracerebral hemorrhage

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Background and aims: Management of patients with supratentorial intracerebral hemorrhage (SICH) remains controversial. Some studies showed that selected patients may benefit from large decompressive craniectomy (DC), instead of craniotomy with hematoma evacuation. Our aim is to describe our population and compare outcomes of both surgical techniques.

Methods: Retrospective analysis of clinical records from patients admitted at our center with SICH between January 2006 and October 2016 that underwent surgery. T-student and chi-square tests were used to compare continuous and categorical variables. Shift analysis was applied to compare outcomes of both surgical groups.

Results: 42 SICH patients (29 men, mean age 52) were operated, 10 of which underwent DC in addition to hematoma evacuation. There were no differences between groups regarding vascular risk factors, anticoagulation, baseline blood pressure or GCS score, hematoma location, intraventricular rupture or pre-op midline deviation, bleeding etiology, surgical reintervention or complications. The group requiring DC had lower alcohol abuse (0% vs. 32%, $p=0.05$), lower INR (1.1 vs. 2.2, $p=0.041$) and lower HASBLED score (0.6 vs. 1.6%, $p=0.011$). Shift analysis of mRS score and GOS score at 12 months revealed a worse outcome for DC patients ($p=0.055$ and $p=0.061$).

Conclusion: Our work shows that most SICH patients were not elected for DC and the small number of patients in this group is a limitation of the study. Since patients were not randomly assigned to the procedures, one must be cautious when interpreting the worse functional outcome of DC patients, since they might have a worse pre-op prognosis.

Disclosure: Nothing to disclose

EP3016

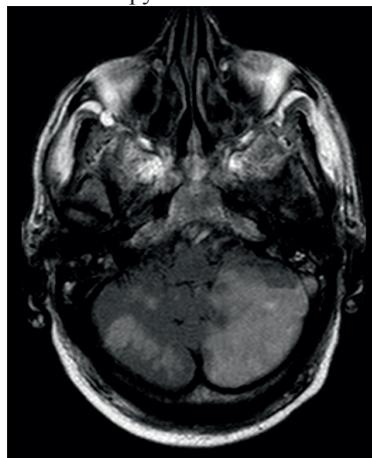
Bilateral vertebral artery occlusion resulting from giant cell arteritis: A case report

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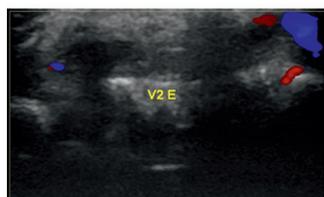
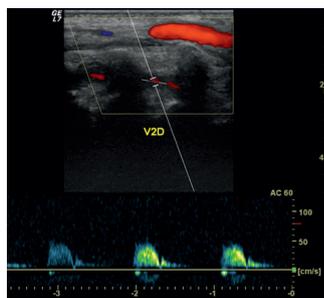
Background and aims: Giant cell arteritis (GCA) is a systemic vasculitis which mostly affects large and medium-sized arteries. Bilateral vertebral artery occlusion (BVAO) is rare and it usually results from atherosclerotic disease; however it can also be influenced by the inflammatory process, related with higher mortality rates.

Methods: Diagnostic evaluation and short-term follow-up of a patient admitted in neurology department.

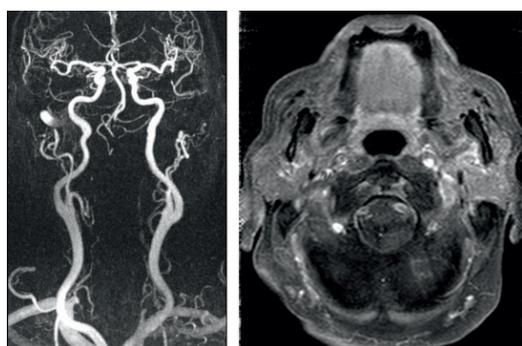
Results: An 86-year-old Portuguese man was admitted in neurology department with imbalance on walking, recurrent vomiting, progressive clinical deterioration, prostration and severe weight loss, beginning three months ago. Neurological exam revealed temporal and spatial disorientation without impairment of other higher functions, cranial nerves or muscle strength. Patient was unable to walk due to postural instability. Temporal artery pulses were present and symmetric, with no pain or induration on palpation. Many diagnostic examinations were performed: blood tests revealed normocytic normochromic anemia and high erythrocyte sedimentation rate (86 mm/h); CT scan showed subacute bilateral cerebellar infarction; cervical and transcranial doppler ultrasound showed BVAO with diffuse wall thickening suggestive of arteritis; Angio-MRI confirmed vertebral artery occlusion and peripheral concentric linear capture, supporting an inflammatory process in the artery wall. Temporal artery biopsy confirmed GCA. General condition and neurological deficits have gradually improved after early administration of corticotherapy.



Bilateral cerebellar infarction (T2 FLAIR)



Bilateral vertebral artery occlusion (V2D and V2E)



Left: non-filling of vertebral arteries; Right: peripheral concentric linear capture.

Conclusion: A few cases of BVAO in the context of GCA are described; however causality between these two entities cannot be demonstrated easily. In this case report, the findings suggestive of inflammation in the artery wall support that vasculitis is the main pathogenic mechanism of occlusion and consequent bilateral cerebellar infarction.

Disclosure: Nothing to disclose

EP3017

Cancelled

EP3018

Intracerebral haemorrhage and the role of the inflammatory response

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Background and aims: Spontaneous intracerebral hemorrhage (sICH) has been linked to a systemic inflammatory and stress response, translated by hyperglycaemia and increased neutrophil to lymphocyte ratio (NLR). We determined if these factors affect the prognosis.

Methods: From September to December 2014 we evaluated all the patients admitted to our centre with sICH. Clinical, laboratorial and radiological features were analysed to assess the influence in outcome, defined by mortality at 30 days and functional independence at 90 days (modified Rankin Scale (mRS) ≤ 2).

Results: We included 51 patients. The mortality rate was 40% and 74% had mRS >2 at 90 days. Higher mortality and long term dependence were associated with low Glasgow Coma Scale score at entrance (both $p<0.001$), higher systolic blood pressure (respectively $p=0.008$ and 0.005), glucose level (both $p=0.001$), NLR ($p=0.132$ and 0.008), larger haematoma ($p<0.001$ and 0.082) and intraventricular blood ($p=0.07$ and 0.021). In a multivariate logistic regression model, hyperglycaemia (beta=1.02, IC95% 1.01 – 1.05, $p=0.019$) and NLR (beta=1.49, IC95% 1.01 – 1.79, $p=0.046$) were predictors of poor outcome at 90 days, but not mortality ($p>0.05$).

Conclusion: The presence of high glucose level at admittance as well as increased NLR, a probable manifestation of stress response, were predictors of poor outcome in sICH. This could be new target for therapeutic intervention.

Disclosure: Nothing to disclose

EP3019

Antiplatelet usage alters clot density in acute ischemic stroke: A hyperdense middle cerebral artery study

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Background and aims: The hyperdense artery sign on computed tomography is a surrogate of intraluminal thrombus. Clot density can be quantified by means of Hounsfield Units (HU). Here, we explored whether clot density in middle cerebral artery (MCA) occlusion is related to blood constituents and prestroke medication.

Methods: We performed a retrospective review of patients with ischemic stroke admitted within 4.5 h of symptom onset. We assessed the site of MCA occlusion as well as density of the clot in 150 patients. The HU values for the clot were divided with contralateral MCA segment to yield relative HU ratio (rHU).

Results: We found an inverse correlation of rHU with erythrocyte count ($p < 0.001$). Patients on antiplatelets had a significantly higher rHU compared to patients without ($p = 0.024$). Higher rHU was more likely with the use of antiplatelets (OR 4.24, CI 1.10-16.31, $p = 0.036$). Erythrocyte (OR 0.18, CI 0.05-0.55, $p = 0.003$), and thrombocyte counts (OR 0.99, CI 0.98-0.99, $p = 0.029$) were associated with odds for more hypodense clots.

Conclusion: Aspirin alters clot structure in vitro, resulting in the formation of clots with thicker fibers and bigger pores, which subsequently allows better entanglement of erythrocytes and raises the efficacy of thrombolysis. Our study disclosed an effect of antiplatelet therapy on the composition of intracranial clots in the setting of acute ischemic stroke in the anterior circulation. This finding may in part explain the higher success of thrombolysis and better prognosis ischemic stroke in patients on aspirin.

Disclosure: Nothing to disclose

EP3020

Diagnosis challenges in Susac's syndrome: A case report

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Background and aims: Susac's syndrome is a rare neurologic disorder mainly affecting young women aged 20- to 40 years. It consists of a clinical triad including encephalopathy, branch retinal artery occlusions and sensorineural hearing loss.

Methods: We present a case of Susac's syndrome with an atypical delay in symptoms development.

Results: A 41-year-old woman was admitted to the ED due to her acute confusional state. She suffered from sudden bilateral hearing loss and general weakness two days before. Past medical history revealed recurrent retinal artery occlusions in both eyes from 2005 to 2007. Neurological examination revealed a relative afferent pupil defect in right eye and bilateral hearing impairment. She was treated with prednisone and vitamin E without significant improvement. After an extensive investigation including clinical, laboratory and MRI findings including "snowball lesions" in the corpus callosum and periventricular hyperintense lesions, the patient was found to suffer from Susac's syndrome. She was treated with i.v. methylprednisolone. Slow and light improvements were observed.

Conclusion: Patients suffering from SUSAC often present only part of the triad, and there is multisystemic involvement which imitates other more common neurologic disorders such as acute disseminated encephalomyelitis and multiple sclerosis. Our patient does not have at initial presentation all the classical features of the disease. About 10 years separate the first manifestations of the syndrome from the appearance of the other symptoms. MRI imaging characteristics specific to the disease allowed us to rule out of other clinical disorders and avoid delay in treatment.

Disclosure: Nothing to disclose

EP3021

Cancelled

EP3022

Cancelled

EP3023

Soluble urokinase plasminogen activator receptor levels are elevated in stroke and correlated with inflammatory and endothelial markers

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Background and aims: Soluble urokinase plasminogen activator receptor (SUPAR) has been recently described to be not only an important prothrombotic factor but also a sensitive marker of tissues' remodeling and an inflammatory marker, which can be used as an independent prognostic factor in prediction of various cardiovascular events (CVE). Therefore, the aim of our study was to evaluate the level of SUPAR in patients after ischemic stroke, in correlation with inflammatory markers (CRP, PCT, NT-proCNP) and markers of endothelial damage (endothelin 1-21, NT-proCNP).

Methods: The blood samples were collected from 50 patients (mean age 73.7±11.9 years, 26F and 24M), which were admitted to the Department of Neurology due to first-time ischemic stroke episodes. We evaluated the serum level of SUPAR, CRP, PCT, endothelin and NT-proCNP during 1., 3. and 7. day from stroke onset.

Results: The mean level of SUPAR1/2/3 (1./3./7.-day measurement) was 3.43±2.2/3.58±3.0/4.22±3.9 ng/ml. The serum level of SUPAR1/2/3 was strongly correlated with the serum level of PCT1/2/3 (R1=0.96/R2=0.96/R3=0.97, p<0.05) but not CRP (R1,2,3=ns, p>0.05). The serum level of SUPAR was also correlated with the serum level of NT-proCNP1/2/3 (R1=0.78/R2=0.77/R3=0.92, p<0.05). The serum level of NT-proCNP1/2/3 was correlated with the serum level of endothelin 1-21 (R1=0.44/R2=0.49/R3=ns, p<0.05).

Conclusion: The mean serum level of SUPAR in ischemic stroke patients is correlated with serum level of PCT (inflammatory marker) and NT-proCNP (inflammatory and endothelial marker) therefore it should be taken into consideration as a possible prognostic factor of inflammation and endothelial damage in this group of patients.

Disclosure: Nothing to disclose

EP3024

ApoE genotype and the outcome of thrombolysis in acute ischemic stroke

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Background and aims: The apolipoprotein E gene (apoE) influences susceptibility to atherosclerosis. ApoE ε4 is independently associated with lobar intracranial hemorrhage (ICH) and it enhances amyloid deposition in blood vessels, while the ε2 allele predisposes to vasculopathic changes leading to rupture of amyloid laden vessels. Thus, one might expect ε4 and ε2 carriers to have increased susceptibility to ICH, especially in a lobar location.

Aim: to study the impact of the different haplotypes in the outcome of thrombolysis, namely in the development of symptomatic ICH (sICH), recanalization, functional outcome and mortality.

Methods: We included 385 consecutive ischemic stroke patients submitted to recombinant tissue plasminogen activator treatment between January-2011 and March-2015. Admission CT-scans were reviewed to calculate ARWMC, Edema and ASPECTS scores. Patients were followed for up to at least 6 months post-stroke or until death. Outcome measures included evaluation of recanalization on the first 24hours (transcranial color coded Doppler or angio-CT), sICH and assessment of functional outcome at 3 months after stroke (using modified Rankin scale).

Results: Peripheral artery disease, higher uric acid and HDL levels were associated with the presence of at least one ε2 allele. In multivariate analysis, ε2 allele predicts mortality (HR: 1.907, [1.119,3.248], p=0.018). Considering radiologic measures, ε2 allele predicts ARWMC (OR: 2.093, [1.095,4.006], p=0.026).

Conclusion: The main findings of our study is the relationship of apoE ε2 with white matter changes and with a higher mortality rate. No association was found between with either allele and the predefined thrombolysis outcomes.

Disclosure: Nothing to disclose

Cerebrovascular diseases 8

EP3025

Reorganization of cerebral hemodynamics in patients with arteriovenous malformations

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Background and aims: Although there are many works devoted to this problem, particularities of cerebral hemodynamic in patients with arteriovenous malformations (AVM) are poorly described.

Aims: Research the influence of arteriovenous shunting at the reorganization of cerebral hemodynamics in patients with AVM.

Methods: Between 2005 and 2016 years 357 consecutive patients with brain AVM were treated in Dnepropetrovsk regional hospital. We conducted a comprehensive clinical, neuropsychological and neuroimaging examination of this subjects.

Results: The relative increase of the linear velocity of blood flow (LBV) in the arteries feeding AVM was 143% (145.56 ± 15.57 cm/s). Increasing of blood volume flowing through the AVM lead to significant increasing of total cerebral blood flow till 1679.05 ± 448.03 ml/min (exceeds normal range in 2 times). Lesion of autoregulation was found in 75% of patients with AVM during conducting of functional tests. During hyperventilation LBV decreased in average on $25 \pm 7.4\%$ (significant lower ($p = 0.01$) than normal). Response to hypercapnia was absent in 37.5%. Overshoot ratio in averaged 1.06 ± 0.07 . On computed tomography perfusion the cerebral blood flow (CBF) and cerebral blood volume (CBV) were markedly elevated within the AVM nidus. However, the perinidal areas demonstrated low CBF and CBV, suggestive of perinidal ischemia in follow areas: surrounding AVM-in 91.5%, remotes from AVM in the ipsilateral hemisphere-in 61% of cases; in the contralateral hemisphere - in 34.4%.

Conclusion: We have shown that features of cerebral hemodynamics depends on the structural and functional characteristics of AVM.

Disclosure: Nothing to disclose

EP3026

Low-dose versus standard-dose rtPA in acute ischemic stroke: An explorative single-centre study

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Background and aims: Low-dose rtPA is currently used in Japanese subjects (Yamaguchi, Stroke 2006) with acute ischemic stroke, while it was not shown to be non-inferior to standard dose in a recent trial involving predominantly Asian subjects (Anderson, NEJM 2016). We aimed to evaluate safety and efficacy of low-dose rtPA in a Caucasian cohort of acute stroke patients.

Methods: From our database, among 389 rtPA-treated patients we consecutively selected 19 subjects treated with low-dose rtPA (≤ 0.75 mg/kg), matched by NIHSS score, age and onset-to-treatment time to 38 subjects treated with standard-dose rtPA (0.9 mg/kg). Primary efficacy outcome was defined by favourable 90-days functional outcome (mRS score ≤ 2). Secondary efficacy outcomes were NIHSS score and mRS at discharge. Safety outcome was the proportion of symptomatic ICH (according to SITS-MOST criteria) and death.

Results: Baseline clinical and demographic features were similar between groups. At discharge, low-dose rtPA patients had NIHSS and mRS scores comparable to control group ($p=0.659$; $p=0.520$). Good functional outcome occurred in 47.4% low-dose subjects vs. 52.6% in standard-dose group ($p=0.925$). In addition, the distribution of mRS scores at 90 days was not significantly different between the two treatment groups ($p=0.987$). The proportion of sICH and death similar as well ($p=1.000$).

Baseline clinical and demographic characteristics.

	rtPA dose		p-value
	Standard (N = 38)	Low (N = 19)	
Age (yr)	75.7 (12.12)	75.8 (9.85)	0.859
Gender: male	21/38 (55.3%)	7/19 (36.8%)	0.303
mRS score before stroke	0 (0)	0 (0)	0.939
NIHSS score at stroke onset	13.5 (11.5)	15 (11)	0.799
rtPA dose (mg/kg)	0.9 (0.01)	0.68 (0.12)	0.000
Estimated body weight (kg)	75 (10)	65 (18)	0.050
Time from onset to rtPA administration (min)	141 (57)	165 (46)	0.198
Additional endovascular treatment	4/38 (10.53%)	2/38 (10.5%)	1.000
Final diagnosis			0.243
Other cause of stroke	2/38 (5.3%)	2/19 (10.5%)	
Cardioembolism	17/38 (44.7%)	4/19 (21.1%)	
Dissection	0/38 (0.0%)	1/19 (5.3%)	
Large-artery occlusion	9/38 (23.7%)	3/19 (15.8%)	
Two or more causes	3/38 (7.9%)	1/19 (5.3%)	
Small-vessel disease	1/38 (2.6%)	1/19 (5.3%)	
Cryptogenic stroke	6/38 (15.8%)	7/19 (36.8%)	
Hypertension	26/38 (68.4%)	13/19 (68.4%)	1.000
Diabetes	4/38 (10.5%)	3/19 (15.8%)	0.887
Antiplatelet therapy at stroke onset	20/38 (52.6%)	7/19 (36.8%)	0.399
Dual antiplatelet therapy	1/38 (2.6%)	2/19 (10.5%)	0.529

mRS: modified Rankin Scale. NIHSS: National Institutes of Health Stroke Scale.
rtPA: recombinant tissue plasminogen activator.

For categorical variables, chi-squared test was performed. For numerical variables, Wilcoxon rank-sum test was performed; median and interquartile range are shown.

Table 1. Baseline clinical and demographic characteristics.

Outcomes of study groups.

	rtPA dose		p-value
	Standard (N = 38)	Low (N = 19)	
Primary outcome			
3-months mRS ≤ 2	20/38 (52.6%)	9/19 (47.4%)	0.925
Secondary outcomes			
3-months mRS score	2 (2.75)	3 (2)	0.938
NIHSS score at discharge	5 (12.5)	5 (8.5)	0.659
mRS score at discharge	3 (3.75)	3 (2.5)	0.520
Haemorrhagic transformation	5/38 (13.2%)	3/19 (15.8%)	1.000
Symptomatic intracerebral haemorrhage	2/38 (5.3%)	1/19 (5.3%)	1.000
Death	2/38 (5.3%)	3/19 (15.8%)	0.401

mRS: modified Rankin Scale. NIHSS: National Institutes of Health Stroke Scale.
Wilcoxon rank-sum test was performed; median and interquartile range are shown.

Table 2. Outcomes of study groups.

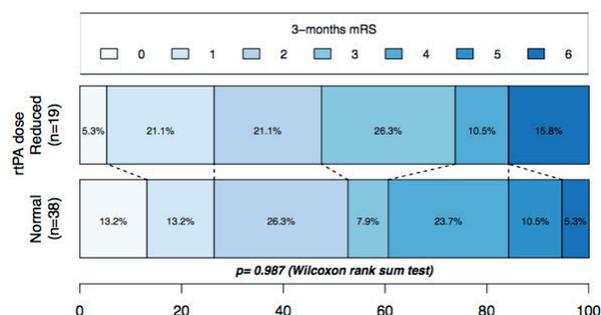


Figure 1. Distribution of 3-months mRS.

Conclusion: Efficacy and safety of low-dose rtPA were comparable to standard-dose rtPA. Due to the small number of patients, the results of this exploratory study cannot be generalized and need to be confirmed in a larger stroke population. However, it appears feasible to consider using low-dose rtPA in frail stroke subjects.

Disclosure: Nothing to disclose

EP3027

Genetic screening in cerebral cavernous malformations: A single center experience

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Background and aims: Cerebral cavernous malformations (CCM) are pathological vascular lesions formed by clusters of dilated capillaries in CNS. CCM may exist in a sporadic form or can be part of a familial autosomal dominant disorder with incomplete penetrance (FCCM). These abnormalities are caused by heterozygous mutations of three genes involved in angiogenesis and endothelial permeability: KRIT1, CCM2, or PDCD10. The main clinical manifestations are headache, seizures, focal neurological deficits and cerebral haemorrhage.

Methods: 21 patients from 13 families over a four years period underwent genetic screening at Policlinico Hospital in Milan. Multiple malformations ($n \geq 2$) and/or a positive familial history of cerebral angiomas were mandatory to perform genetic analysis. We analyzed all exons and intronic boundaries of KRIT1, CCM2 and PDCD10 by Sanger sequencing. MLPA analysis with commercially available kits was used to detect large-scale rearrangements. RT-PCR analysis using cDNA retrotranscribed from blood leukocytes RNA evaluated the functional effects of the candidate variants.

Results: We established a molecular diagnosis in 10 independent probands (76.9%) of our cohort. We found nine independent mutations, four of which not previously described. In 4 familial and 3 sporadic cases we found causative mutations in KRIT1. CCM2 mutations were detected in 2 familial and 1 sporadic case. Segregation test was positive in familial cases. No mutation was found in PDCD10.

Conclusion: A firm diagnosis was established in 76.9% of our cohort using MRI followed by molecular analysis of KRIT1 and CCM2. These results give us the opportunity to undertake future therapies.

Disclosure: Nothing to disclose

EP3028

Cancelled

EP3029

The association between homocysteine and carotid restenosis after endarterectomy: A meta-analysis

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Background and aims: Carotid endarterectomy (CEA) is an effective treatment for symptomatic and asymptomatic patients with high-grade extra cranial carotid stenosis. However, its efficacy is dependent also by the maintaining of the arterial patency. Even if restenosis after CEA is uncommon, its occurrence could increase the risk of cerebrovascular accidents. The cause of this condition could be related with miointimal hyperplasia also sustained by atherosclerotic process. Homocysteine has been identified as a potential risk factor for atherosclerosis. For this reason, we conducted a meta-analysis to investigate the association between homocysteine levels and the risk of restenosis after CEA

Methods: We performed a literature search in the three main databases (PUBMED/MEDLINE, EMBASE, COCHRANE). We identified 4 main trials investigating the role of homocysteinemia as risk factor for carotid restenosis. We performed a meta-analysis using Hedges g statistic as a formulation for the standardized mean difference under the fixed effects model.

Results: A total of 562 patients were included in the analysis (116 with carotid restenosis – 19% of total). We did not observe a statistical association between homocysteine levels and the risk of carotid restenosis after CEA (SE for fixed effects: 0.112; p: 0.708). Test for heterogeneity showed a Q: 5.12 with I² of 61% (p: 0.07).

Conclusion: Hyperhomocysteinemia did not represent a risk factor for early restenosis after CEA. However, further studies with standardized methodology of laboratory tests and radiological evaluation of restenosis degree are required.

Disclosure: Nothing to disclose

EP3030

New approach to evaluation of stroke risk: Modification of social predictors

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Background and aims: The strategy of prevention of stroke is based on the detection and correction of stroke risk factors. However, descriptions of external (or social) risk factors of stroke are poorly presented in scientific researches and publications, although they play a significant role in the autoregulation of cerebral circulation.

Our objective is to study the spectrum of social risk factors and their impact on the incidence of different subtypes of cerebral ischemic stroke.

Methods: We have examined 140 patients with ischemic stroke (average age -65.2±8.7 years) using clinical and instrumental methods, laboratory examination and detailed clinical and anamnestic survey. 45 patients without stroke (average age -63.3±3.1 years) were included in control group. Among known social predictors of development of cerebral ischemia we discover 7 risk factors with higher incidence and use them to evaluate risk of cerebral stroke with help of specialized social risk of stroke scale (SSRS).

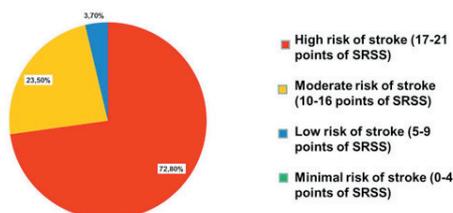
Occurrence of social predictors of ischemic stroke (%)

Social factors	Groups of patients	
	A1 (n = 140) %	A2 (n = 45) %
Sleep disturbance	100	24,4
Excessive stress	100	31,1
Abnormal night activity	100	11,1
Long-term work with monitors	87,9	35,5
Physical inactivity	85,8	11,1
Meal problems	75,0	24,4
Alcohol, smoking	70,0	6,6
Marriage	70,0	84,4
Physical hard work	62,1	46,6
Overtheat	57,1	40,0
Miss of antihypertensive drugs	57,8	40,0
Constant travels by plane	46,4	24,4
No sex	37,1	17,7
Depression	17,9	11,1

Occurrence of social predictors of stroke

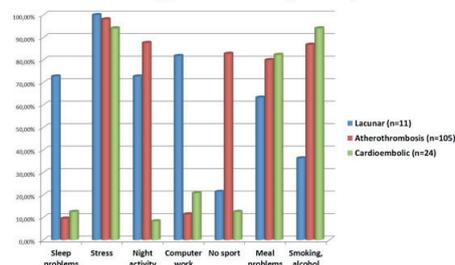
Results: Adequate correction of predictors has resulted in 13.5% of decreasing of risk of stroke incidence (2 years of observation). The incidence of lacunar stroke was tied with excessive stress, high nocturnal activity, long-term work with monitors and irregular meals. Atherothrombotic stroke was connected with excessive stress, sleep disturbance, reduced physical activity, irregular meals and smoke and alcohol addiction. Cardioembolic stroke subtype was associated with excessive stress, smoking and irregular meals.

Social risk of stroke evaluation (n=140)



Evaluation of stroke risk

Association of social predictors with subtype of stroke (n=140)



Association of predictors with stroke subtype

Conclusion: Discovered complex of social risk factors of stroke will allow clinicians to define patients with high risk of stroke and to develop an appropriate strategy of individual prevention.

Disclosure: Nothing to disclose

EP3031

Cancelled

EP3032

A case of direct carotidocavernous fistula after mechanical thrombectomy in acute stroke: Case report

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Background and aims: Mechanical thrombectomy is now the advance treatment in acute large vessel occlusion. The complications after thrombectomy are variety.

Methods: We purpose an interesting case of direct carotidocavernous fistula (CCF) after thrombectomy.

Results: Case: A 76 years old man presented with sudden left hemiparesis for 3 hours. He was administrated with intravenous thrombolysis but clinical not improved. The MRA brain showed right proximal M1 occlusion. Then, he was sent to mechanical thrombectomy using stent retriever for 3 times. Control angiogram showed complete recanalization of right M1 (TICI 3) and small tear vessel at right internal carotid artery (ICA) and right cavernous sinus with blood flow drained to right inferior petrosal vein, right sphenoparietal sinus but not seen drained in ophthalmic vein, so called direct CCF. We decided to observe this CCF and clinical of stroke. His clinical improved, power motor from grade 0 to grade 3. He stayed in hospital for 2 weeks with no clinical of direct CCF. Two months later, he developed the clinical of direct CCF with proptosis, chemosis, limit extraocular muscle movement and ophthalmic bruit at right eye. He was sent to transvenous embolization using fiber coils at right cavernous sinus. Twenty-four hours after procedure, his clinical of direct CCF significantly improved and turn to normal within 2 weeks.

Conclusion: Direct CCF is a rare complication from mechanical thrombectomy that endovascular devices injured the cavernous segment of ICA. It can be treated by transvenous coil embolization or transarterial detachable balloon embolization.

Disclosure: Nothing to disclose

EP3033

Case report of a patient with symptomatic, bilateral, gigantic extracranial carotid artery aneurysms and the accompanying multimodality imaging findings.

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Background and aims: We are reporting the case of a patient with stroke related to bilateral, gigantic extracranial carotid artery aneurysms (ECCAs), with significant mural thrombus affecting both carotid bifurcations. Aneurysms of the common carotid artery are a rather rare condition, and a bilateral presentation increases additionally the sparseness of such a finding.

Methods: A 59-year-old male developed an acute symptomatology corresponding to a left hemispheric stroke. The neurological examination revealed dysarthria, paresis of the lower part of the right facial nerve (VII cranial nerve), right hemihypesthesia, right hemiparesis (2/5 on upper and 1/5 of lower limb of the MRC Scale) and right Babinski sign. His medical history included smoking, mild consumption of alcohol and hypertension. Multimodality imaging (on contrast-enhanced ultrasound (CEUS), Multidetector Computed Tomography Angiography (MDCTA) and contrast-enhanced Magnetic Resonance Angiography (MRA) revealed the bilateral presence of ECCAs.

Results: Due to the presence of mural thrombus, the patient was initially treated with both anticoagulant and antithrombotic agents and, in second phase, with surgical reconstruction of the carotid axis (with aneurysmatectomy, graft interposition and ligation of the external carotid arteries), without any complications.

Conclusion: Bilateral aneurysms of the common carotid artery are an extremely rare condition, with an unclear etiology. Review of recent literature showed a possible shift in etiology of ECCAs. Previous studies reported domination of atherosclerotic aneurysms, while recent ones reveal an increase in the frequency of post-carotid endarterectomy (CEA) aneurysms, highlighting the importance of post-surgical monitoring, in order to prevent permanent neurological deficits.

Disclosure: Nothing to disclose

EP3034

Poor outcome after complete recanalization with mechanical thrombectomy in acute basilar artery occlusion: Two cases

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Background and aims: Basilar artery occlusion (BAO) is a rare but potentially fatal cause of stroke. BAO may lead to death or long-term disability if not promptly recanalized. After many positive results in thrombectomy trials of anterior circulation ischemic stroke, the question arises whether these positive results may also be applied to the patients with basilar artery occlusion.

Methods: We report two cases of 38-64-year-old male patients presented with acute BAO who underwent endovascular thrombectomy.

Results: Clinical presentation: Two consecutive patients admit emergency department with posterior circulation symptoms. Cranial CT was normal whereas DWI revealed acute ischemic infarct at basilar artery territory. NIHSS was 6 - 24 and GCS was 12-8, respectively. Their CTA showed middle-distal basilar artery occlusion. The patients were underwent mechanical thrombectomy by using stent retriever within 6 hour of symptoms onset. Despite complete recanalization according to TICI scale system, neurological signs progressed and patients transferred to neurointensive care unit. One patient was unconscious, tetraparetic and depended on mechanical ventilator who had hemorrhagic transformation on control CT at 24 hour. Brain death occurred in the other patient at the 22nd day.

Conclusion: Mechanical thrombectomy with stent retrievers yielded high recanalization rates in BAO patients and good outcomes in approximately 1/3 of patients. As in our cases some patients have poor prognosis despite complete recanalization at eligible time window. Serebral microcirculation and collaterals, length of thrombi, initial infarction severity and technical devices may be important predictors and has to be kept in mind for good outcome beside early recanalization.

Disclosure: Nothing to disclose

EP3035

Prognostic factors of functional outcome after surgical treatment of putaminal hemorrhages

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Background and aims: The purpose of this study was to investigate the factors affecting the functional outcome in patients after surgically treated putaminal hemorrhages. Surgery for putaminal hemorrhages remains a controversial issue. Although numerous reports describe conflictive results regarding short-term outcome of surgically treated patients, very little is known about their long-term functional outcome.

Methods: We evaluated the data of 58 patients who underwent open surgical evacuation of putaminal hematomas admitted to a metropolitan hospital in southern Taiwan from January 2009 to December 2015. Patients were categorized into 2 groups based on their modified Rankin Scale (mRS) after 6 months from onset. Various presumptive prognostic factors were analyzed to investigate relationships between various clinical characteristics and outcomes.

Results: Of the enrolled patients, 11(19%) showed a mRS of 0-3, and were categorized as the good outcome group, while another 47(81%) patients showed a mRS of 4-6 and were categorized as the poor outcome group. (Table 1) By univariate analyses, poor outcome was associated with old age, poor initial GCS score, volume of parenchymal hematoma, presence of intraventricular hemorrhage (IVH), hydrocephalus and modified intracerebral hemorrhage (MICH) score. By multivariate analysis, among the factors above, old age and MICH score were independent prognostic factors for poor outcome

Table 1. Factors for functional outcome by univariate analysis

Variable	Good outcome mRS: 0-3 (n=11)	Poor outcome mRS: 4-6 (n=47)	p-value
Age, y(mean ± SD)	48.7 ± 9.3	59.0 ± 13.0	0.007
Gender (F/M)(n%)	4/7(63.6)	36/11(21.6)	1.000
Hypertension, n (%)	6	34	0.290
DM, n (%)	1	7	1.000
Plasmin inhibitor, n (%)	0	0	0.985
GCS (mean ± SD)	10.1 ± 2.1	7.5 ± 2.5	0.003
Pupil, loss of light reflex, n (%)	1	20	0.044
ICH volume, ml (mean ± SD)	36.97 ± 11.51	51.46 ± 28.51	0.021
Lah side, n (%)	4	23	0.607
Midline shift, n (%)	7	38	0.244
Intraventricular bleed, n (%)	3	32	0.038
Hydrocephalus, n (%)	2	32	0.005
Hematoma involved thalamus n (%)	0	10	0.142
Hematoma involved caudate, n (%)	0	7	0.327
MICH score			0.011
1	2	2	
2	6	11	
3	3	11	
4	0	21	
5	0	2	

Table 1

Conclusion: In patients who have large amounts of hematoma and require open surgical evacuation, the only significant risk factor for functional outcome are the preoperative GCS score and age. Most of patients with surgically treated putaminal hemorrhages remain dependent and significantly impaired activities of daily life status.

Disclosure: Nothing to disclose

EP3036

Relationship between bilateral occlusion ICA and neurological deficit level in correlation with re-established collateral flow.

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Background and aims: The purpose of this paper is to show relative relationship between bilateral occlusion ICA and neurological deficit level in correlation with re-established collateral flow.

Methods: Out of 2845 patients admitted to the St Sava Hospital in 2016, examined by ultrasound diagnostic equipment, bilateral occlusion ICA was identified in 14 patients : M/F:12/2; average age 67. Clinical protocol included NIHSS examination, Colour Doppler flow imaging, TCD, MSCT or MR. Dominant risk factors were hypertension in 8; smoking in 10; hyperlipidemia in 4; and heart disease in 5/14 patients.

Results: Bilateral occlusion ICA was registered in 11 ; bilateral occlusion CCA in 3 patients. Collateral flow over Willis' circle from VB vessels to bilateral ICA vessels over PCoA was bilaterally registered in all 14 patients. Collateral flow over ECA-ICA ipsilateral anastomosis was bilaterally registered in 11 (with occlusion of both ICA). Flow was not registered through bilateral OA in 2 patients (with bilateral occlusion CCA). Neurological deficit unilaterally as hemiplegia was registered in 3 patients, medium to high level hemiparesis in 2, and low level hemiparesis in 9 (mobile) patients. Dominant finding on MSCT (MR) was bilateral lacunar ischemia (9/14 patients).

Conclusion: Bilateral occlusion ICA is found more often in male patients with hypertension and smoking as main risk factors. Activation of collateral cerebral circulation over ECA-ICA anastomosis, as well as over Willis' circle, makes distal cerebral perfusion sufficient. This has a minor neurological deficit as a consequence, with lacunar ischemic lesion as the dominant finding on MSCT (MR) of endocranium.

Disclosure: Nothing to disclose

Child neurology/developmental neurology

EP3037

Can serum levels of C-reactive protein (CRP), Interleukin-6 and copeptin discriminate between simple and complex febrile seizures?

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Background and aims: To evaluate serum levels of C-reactive protein (CRP), Interleukin-6 (IL-6) and copeptin in children with febrile seizure (FS) and their ability to discriminate between simple (SFS) and complex FS (XFS). **Methods:** The study included 80 febrile children; 40 did not develop febrile seizure (FC), 29 developed SFS and 11 developed XFS. The study also included 10 healthy children as negative control (NC). Clinical evaluation included full history taking, general examination and neurological examination to evaluate patients' general conditions and to confirm inclusion criteria. On admission; body temperature was measured and a venous blood sample was obtained for determination of complete blood count (CBC.) and ELISA estimation of serum CRP, IL-6 and copeptin.

Results: Male-to-female ratio was 2.64:1 and frequency of family history of FS was 17.5%. At admission; body temperature was significantly higher in febrile patients with significantly higher temperature in FS patients than in FC patients. Serum CRP, IL-6 and copeptin levels and TLC were significantly higher in febrile patients compared to NC children and in FS patients compared to FC patients. Receiver operating characteristic (ROC) curve analysis defined high serum copeptin, IL-6, CRP, at admission body temperature, low Hb. Conc. and high total leucocytic count (TLC) as predictors for FS, in decreasing order of significance. Regression analysis defined high serum copeptin and IL-6 as the persistently significant predictors for FS among febrile patients and XFS among FS patients, respectively

Conclusion: Elevated serum levels of copeptin and IL-6 could discriminate febrile children susceptible to develop seizure. Elevated serum IL-6 could discriminate patients liable to develop XFS

Disclosure: Nothing to disclose

EP3038

Neurological and psychological characteristics of children with connective tissue dysplasia

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Background and aims: To study the clinical manifestations of cerebral venous insufficiency and psychological status in children with connective tissue dysplasia.

Methods: The main group consisted of 60 children with signs of connective tissue dysplasia in age from 10 to 16 years. The comparison group consisted of 40 healthy children. Psychological status was assessed by 20-MFI, CES-D, STAI, EPI.

Results: In the group of patients with connective tissue dysplasia were more common following symptoms: headache in the morning - 88% (group 2 - 29%), increased headaches during sleep with a low headboard - 55% (group 2 - 0%), sleep disturbances - 75% (group 2 - 44%), the noise in my head - 38% (group 2 - 0%), a feeling of nasal congestion - 50% (group 2 - 0%), injection sclera - 64% (group 2 - 12%), venous reticulum on the front surface of the chest - 100% (group 2 - 12%). In group 1 was detected higher levels of total (group 1: 45.9±2.89; group 2: 25.9±3.5) and physical fatigue (group 1: 43.4±3.76; group 2: 24.9±2.3). In group 1 had higher level of depression (group 1: 26.4±2.3; group 2: 12.3±4.5).

Conclusion: Children with severe manifestations of connective tissue dysplasia more often revealed signs of cerebral venous insufficiency than children without the disease. In children with connective tissue dysplasia more pronounced general and physical fatigue, as well as has a tendency to depressive disorders.

Disclosure: Nothing to disclose

EP3039

Expanding neuroradiological spectrum of Rubinstein Taybi syndrome: report of a case

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Background and aims: Rubinstein-Taybi syndrome (RTS) is a rare genetic disorder mainly caused by heterozygous mutations of the CREBBP (cAMP-response element binding protein) gene (16p 13.3). RTS is characterized by growth retardation, facial and limb dysmorphies and microcephaly with neurocognitive dysfunction. Epilepsy occurs in about 25% of cases. Brain MRI abnormalities are reported in a variable percentage of patients, involving corpus callosum, posterior periventricular white matter and posterior fossa; rarely, gyration abnormalities such as pachygyria and polymicrogyria have been reported. We report a case of a patient with an MRI pattern of bilateral superior temporal gyrus cortical dysplasia.

Methods: A 22-year-old was diagnosed with RTS at the age of 4 based on typical dysmorphies: broad thumbs and big toes, downward slanting palpebral fissures, microcephaly. Severe mental retardation, autism, hypoacusia and hypotonia were also noted on the neurological examination. Pharmacoresistant partial and generalized seizures started at 2 years.

Results: Sequencing of CREBBP gene revealed a de novo mutation in exon 27 (substitution c.4508A>T, p. Tyr1503Phe). Brain MRI with gadolinium performed at 6 years documented poor grey-white matter differentiation and abnormal gyral anatomy with hyperintensity of the sub-cortical white matter at the superior temporal gyri bilaterally (double ECHO). The corpus callosum was normal.

We were not able to find in literature the peculiar cerebral malformation we found in our patient.

Conclusion: The causal mutation impairs transcriptional regulation by damaging, in particular, neurogenesis and differentiation of the cortical neural progenitor cells. We think that cortical dysmorphologies in RTS are more frequent than expected based on literature reports.

Disclosure: Nothing to disclose

EP3040

Intranasal oxytocin administration reduces memory, anxiety and depression-related deficits in a valproic acid-induced perinatal model of autism

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Background and aims: Lately there is an increased interest for the beneficial effect of the intranasal oxytocin in the neuropsychiatric disorders, including autism. Also, one important animal model of autism in rodents is based on the perinatal administration of valproic acid. Thus, we studied the relevance of intranasal oxytocin administration in this valproic acid-induced rat model of autism, as tested on some behavioural tasks relevant for memory, anxiety or depression-like manifestations.

Methods: The model of autism was induced through the intraperitoneally administration of valproic acid (500mg/kg) in the 12.5 day of gestation. The offspring were weaned on postnatal day 21 and after that male animals (n=15) received intranasally administrated oxytocin (Sigma) for 10 consecutive days (20IU), while controls received intranasal saline (3 groups: control, valproic acid and valproic acid+intranasal oxytocin). Memory functions were tested through Y-maze, anxiety behaviour through elevated-plus-maze, while depression was analyzed through the forced-swim-task, during the last 3 days of treatment (days 8, 9 and 10).

Results: We showed an increased in the immediate working memory (e.g.spontaneous alternation behavior) in the valproic acid+intranasal oxytocin group, as compared to valproic acid alone in the Y-maze test. Moreover, the time spent in the open arms of the elevated-plus-maze and the mobility time in the forced-swim-test were increased in the valproic acid+intranasal oxytocin group, as compared to valproic acid alone rats, suggesting facilitatory effects in anxiety and depression-related behaviours.

Conclusion: 10 days of intranasal oxytocin administration in a valproic acid-induced rat model of autism seems to reduce some associated memory, anxiety and depression-related deficits.

Disclosure: This work is supported by a PN-II-RU-TE-2014-4-1886 grant called "A complex study regarding the relevance of oxytocin administration in some animal models of neuropsychiatric disorders", number 120 from 01/10/2015.

EP3041

A rare case of H1N1 triggered recurrent acute necrotizing encephalopathy associated with RANBP2 mutation

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Background and aims: Acute necrotizing encephalopathy (ANE) is a rare disorder presenting with rapidly progressing encephalopathy, usually preceded by a virus-associated febrile illness. While most cases are sporadic and nonrecurrent, familial recurrent ANE due to mutations in the Ran Binding Protein 2 (RANBP2) gene have been recently reported.

Methods: We report the clinical course of a Portuguese child with recurrent ANE.

Results: A 4-year-old boy, with a previous history of encephalopathy due to ANE at the age of 5-months with residual language domain deficit and right motor hemiparesis, developed reduced consciousness and seizures following a febrile respiratory infection. Seizures were refractory to first and second antiepileptic drugs and he was sedated with midazolam. His EEG revealed mild background slowing and left temporal slow waves. Brain magnetic resonance imaging showed symmetric multifocal lesions involving bilateral thalami, brainstem, cerebellum and external capsules, consistent with ANE. Cerebrospinal fluid (CSF) examination revealed mildly elevated protein concentration and oligoclonal bands. Remaining investigation identified a positive polymerase chain reaction for human herpesvirus 7 (HHV-7) in CSF and influenza A H1N1 in bronchoalveolar lavage. He was treated with oseltamivir and high-dose steroid therapy followed by oral tapering. He recovered gradually with no de novo deficits. There was no family history of ANE. Genetic testing identified a missense mutation p.Thr585Met in the RANBP2 gene.

Conclusion: To our knowledge, this is the first reported case of recurrent ANE in Portugal. This report emphasizes the need for increased awareness and earlier recognition, since prophylaxis and symptomatic management of infections may be beneficial.

Disclosure: Nothing to disclose

EP3042

Features of the etiological structure of encephalitis in children in the Stavropol region

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Background and aims: Early diagnosis and timely adequate causal and pathogenetic treatment reduces the risk of severe consequences of infectious diseases of the brain. The study of etiological structure of encephalitis presented an interest.

Methods: We conducted dynamic observation of 66 patients (2 months-16 years) with encephalitis. Conducted direct microscopic, bacteriological, mycological study of CSF biological material.

Results: It is established that serious infectious diseases of brain tissue were caused both by bacterial and viral monoinfection and associated pathogens. Viral encephalitis was detected in 45 (68.2%) patients. Among patients with established etiology, predominance of monoinfection was observed (90%) over mixed infection. In mixed infection the pathological process was caused by a combination of herpes simplex virus enterovirus, cytomegalovirus. Monoinfection was caused by enterovirus (44.4%), herpes simplex virus (37%), the virus Varicella Zoster (14,8%), cytomegalovirus (3.7%). In 28.9% of cases occurring with involvement of the meninges (unknown etiology and enterovirus). Bacterial encephalitis (31.8%) in 100% of cases proceeded with meninges involvement. In 52.4% of cases monoinfection of H. infl., Str. pneum was observed, in 28.6%-mixed infection (bacterial-fungal, viral-bacterial, including-Mycobacterium tuberculosis), 19% - of unidentified etiology. Among patients with bacterial encephalitis rural areas prevailed. Patients with encephalitis of unknown etiology received at different times from the onset of the disease, which had an impact on the verification of the etiological diagnosis.

Conclusion: To improve the quality of etiologic diagnosis it is necessary to organize early hospitalization of patients with suspected neuroinfection in specialized hospitals of the Regional center.

Disclosure: Nothing to disclose

EP3043

From chronic recurrent headache to leukodystrophiesA. Potic¹, D. Di Bella², E. Salsano², F. Taroni²¹Department of Neurology, Medical Faculty University of Belgrade, Belgrade, Serbia, ²IRCCS Foundation, "C. Besta" Neurological Institute, Milan, Italy

Background and aims: Migraine is the most common recurrent headache in children and young adults. Little is known about the comorbidity of migraine and inherited white matter disorders. We investigated the accidental detection of leukodystrophies among patients with migraine.

Methods: The study comprised 400 patients referred to our Centres over the last six years because of the chronic recurrent headaches. The age of the patients ranged from 5-25 years. In all the patients the headache was the only presenting symptom at admission. Neurologic and neuro-ophthalmologic examination, psychological evaluation, evoked potentials, and radiological studies (CT, MRI, and MRA) were performed in all the subjects. Some underwent also further investigations: metabolic, cardiac, endocrine, and genetic analyses.

Results: In 270 out of the 400 studied patients the headache fulfilled the required diagnostic criteria for a migraine. Of note, among the 270 migraineurs the leukodystrophies were diagnosed in 5 patients (1.85% of the examined migraineurs): Alexander Disease (a 15-year-old male), X-linked Adrenoleukodystrophy (a 24-year-old male), Vanishing White Matter Disease (two females: age 21 years, and 25 years), Pol III-related Leukodystrophy (a 9-year-old male). In the absence of neurologic abnormalities, the neuroimaging and genetic findings revealed the proper diagnosis. The observed interval between the onset of migraine and distinctive clinical features of the leukodystrophies was 1-4 years.

Conclusion: Migraine may precede the typical neurologic signs of leukodystrophies. In patients presenting solely with chronic recurrent headaches, MRI of the brain and genetic analyses can identify a leukodystrophy months/years before the onset of overt leukodystrophy-related symptoms.

Disclosure: Nothing to disclose

EP3044

Mesenchymal chondrosarcoma as a rare cause of lumbar pain in a pediatric patient: a case report.K. Prus¹, J. Barycki¹, A. Szewczyk¹, E. Zienkiewicz², B. Golebiowska², K. Mitosek Szewczyk¹¹Neurology, Medical University of Lublin, Lublin, Poland, ²Neurology, Children's University Hospital, Lublin, Poland

Background and aims: Prevalence of low back pain in pediatric patients ranges widely from 9% to 66% depending on the source population and definition of pain. It has been accepted that back pain in children is connected with highly possible organic etiology. Researches have shown, that MRI may reveal presence of significant pathology in around 25% of cases. In patients with prolonged history of back pain and those presenting significant neurological examination findings, neuroimaging needs to be used at all times to exclude severe and life-threatening conditions that need immediate intervention.

Methods: We present a case of 17-year-old female patient with a few weeks' history of back pain, headache and nonspecific bladder disturbances. No muscle weakness, deep tendon reflexes abnormalities or significant sensation disturbances were present.

Results: A CT scan revealed a tumour mass originating in S1 and S2. MRI confirmed presence of unevenly contrast-enhanced tumour, expanding into spinal canal and compressing dural sac. Patient was immediately admitted to an orthopedic department to perform laminectomy and tumour resection, followed by an adjuvant chemotherapy.



1. MRI scan (T1 sagittal) - tumour mass in sacral area



2. MRI scan (T2 sagittal) - tumour mass in sacral area

Conclusion: Primary CNS mesenchymal chondrosarcomas are rare, with several cases reported in intraspinal locations. Key elements in patient's health history that should raise index of suspicion for neoplastic diseases include presence of neurologic symptoms as well as systemic complaints - fever, weight loss or night pain. Only contrast enhanced MRI scans allow a precise assessment of neoplastic lesions in this area. Appropriate and prompt clinical workup leads to earlier diagnosis and management of tumours causing back pain.

Disclosure: Nothing to disclose

EP3045

Eyelid myoclonia with or without absences: an under diagnosed epileptic syndrome in the Arab Gulf region?

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Background and aims: The clinical manifestations of eyelid myoclonia can be observed in idiopathic, symptomatic or epileptic syndromes. Epilepsy with eyelid myoclonia (EMA) or Jeavons syndrome is considered a form of idiopathic generalized epilepsy. A series of patients showing homogeneous electroclinical features, including eyelid fluttering and typical EEG pattern. Many times, cases of EMA can be missed when video/EEG cannot be obtained and/or clinical ictal phenomena are minimal.

Methods: Children with electroclinical criteria of EMA were retrospectively identified and followed-up with sleep and awake EEGs between April 1995 to July 2016 who visited four hospitals/epilepsy centers in Saudi Arabia and United Arab Emirates.

Results: Ten patients who fulfilled the criteria for EMA were identified, 7 were females, and 3 were males. The age of onset was from 2 years and 4 months to 9 years. The manifestations of EMA included mild impairment of consciousness, rhythmic myoclonic jerks without evident tonic contraction of the upper extremities in 6 patients, and 2 cases presented with versive seizures with deviation of head and body to one side. A twin presented with continuous flutter of eyes and their EEGs showed consistently the phenomenon of fixation-off sensitivity (Figure 1). The ictal EEG consisted of rhythmic, bilateral, synchronous and symmetrical, 3 Hz spike and wave discharges in all patients.

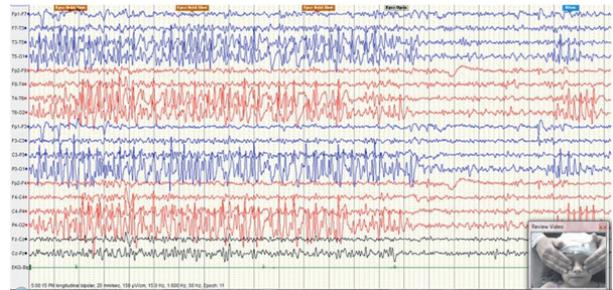


Figure 1. 6.5-year-old Emirati twin II with eye lid myoclonia. Fixation-off sensitivity suspected when high-voltage bilateral occipital epileptiform discharges appeared when her eyes were held closed and persisted as long as her eyes were closed. Low-cut filter, 1.6 Hz; high-cut filter, 70 Hz.

Conclusion: Video EEG is consequently of paramount importance in the diagnosis of EMA, as the opinion of the author that the condition is underrecognized, at least in the Arab Gulf region, as Video EEG is not routinely applied for pediatric population with epilepsy.

Disclosure: Nothing to disclose

EP3046

Cancelled

EP3047

Autonomic cardiac control system response to walking task and executive cognitive task in children with acquired brain injury and typically developed controls

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Background and aims: Children with acquired brain injury (ABI) present dysfunction in a range of physical executive cognitive as well as cardiac autonomic control system (CACS) dysfunctions.

Aim: To examine the CACS response to an executive task, to walking, and to a combined walking and executive task in children with ABI and typically developed (TD) controls.

Methods: 17 children (11-18 years) with ABI, in an active rehabilitation process and had independent walking capability. The control group consisted of 18 age and gender-matched TD children. A Polar RS800CX device was used for assessing heart-rate-variability (HRV), walking endurance assessed by the Six-Minute-Walk-test and executive cognitive function was assessed using the Behavior Rating Inventory of Executive Function questionnaire. The study includes four trials: A five-minute walk on a treadmill set at the average speed measured in the 6MW test, a cognitive manipulation using the Digit Span Backward test at rest, while walking on the treadmill, and during the recovery period post-walking on the treadmill.

Results: Children with ABI presented higher heart rate and lower HRV measures at rest (P -value <0.01). A significant interaction effect was found between the groups; walking on the treadmill has a significant smaller effects on HRV parameters in children with ABI as compared to controls ($F_{2,64}=7.9$, $p<0.001$). Interaction effect of cognitive and walking on treadmill task on HR and HRV was noted with no significant between groups effect.

Conclusion: ABI associated with reduce CACS activity at rest and during and after walking training. Performing cognitive task during walking training may modify these differences.

Disclosure: Nothing to disclose

Critical care

EP3048

Precocious Lance-Adams syndrome in comatose survivors after cardiac arrest: early pharmacological management and outcome

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Background and aims: Comatose Cardiac Arrest (CA) survivors frequently develop early myoclonus, viewed as a poor prognostic sign (status myoclonus); however, a small subset may present precocious Lance-Adams syndrome (LAS); they can markedly improve with treatment. Our aim was to review these patients, focusing on pharmacologic management in the Intensive Care Unit (ICU), time to awakening, and long-term prognosis.

Methods: From our prospective CA registry over 10 years (2006 to 2016), we retrospectively identified adult patients with precocious LAS (defined as generalized myoclonus within 7 days with epileptiform EEG within 48 hours after CA). Functional outcome was assessed through Cerebral Performance Categories (CPC) at three months, CPC 1-2 defined good outcome.

Results: We identified 458 patients, 7 of them (1.5%) developed precocious LAS (4 women, median age 57 years). Within 72 hours after CA, normothermia and off sedation, all had preserved brainstem reflexes, localized pain, and showed epileptiform activity and preserved background reactivity on early EEG. All received valproate, levetiracetam and clonazepam as first line; additionally, topiramate was prescribed in 4, pregabalin in 2, piracetam and perampanel in one each. Valproate serum levels were subtherapeutic in 5/6 tested patients, despite maximal doses. Patients started to show awareness after 3-23 days (median 12); at the three months 3/7 had a good outcome.

Conclusion: Precocious LAS needs to be diagnosed and treated soon, because patients may reach a good functional outcome. A combination of highly dosed, mostly large spectrum antiepileptic agents is often necessary. Awakening may be delayed.

Disclosure: Nothing to disclose

EP3049

Evoked potentials as a potential predictive markers of the outcome in severe hemorrhagic stroke patients

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Background and aims: Our goal was to assess the usefulness of the evoked potentials in the prediction of the outcome in severe hemorrhagic stroke patients.

Methods: In 22 patients (13 men, mean age 61.95±11.63) with hemorrhagic stroke (19 intracerebral and 3 subarachnoid hemorrhage) within the 48 hours after admission to neurointensive care unit (NICU), brainstem auditory evoked potentials (BAEP) and somatosensory evoked potentials (mSSEP) of median nerve were performed in every patient. Glasgow Coma Score (GCS), Full Outline of Unresponsiveness (FOUR) were assessed on the arrival and on the day of release. Modified Rankin scale (mRS) was assessed on the day of release.

Results: There was statistically significant negative correlation between GCS at the day of release and BAEP interlatency III-V for the left side ($r_s = -0.444$, $p = 0.039$). BAEP III amplitude for the left side positively correlated with GCS at release ($r_s = 0.435$, $p = 0.049$). SSEP amplitude P14-N18 for the right side negatively correlated ($r_s = -0.453$, $p = 0.034$) with mRS at release. SSEP interlatency P14-N20 for the left side had a negative correlation with GCS at the day of recording ($r_s = -0.448$, $p = 0.036$), GCS at the release ($r_s = -0.542$, $p = 0.009$) and FOUR at release ($r_s = -0.505$, $p = 0.017$). SSEP amplitude P15-N20 positively correlated with GCS and FOUR at the day of recording ($r_s = 0.506$, $p = 0.027$; $r_s = 0.563$, $p = 0.015$, respectively), and GCS and FOUR at release ($r_s = 0.468$, $p = 0.043$; $r_s = 0.583$, $p = 0.009$, respectively), while negative correlation was found with mRS at release ($r_s = -0.457$, $p = 0.049$).

Conclusion: Results of our study indicate that BAEP and mSSEP have potential value in prediction of outcome in hemorrhagic stroke patients.

Disclosure: Nothing to disclose

EP3050

Decompressive craniectomy in acute large cerebral infarction: experience from Chang Gung Memorial Hospital, Kaohsiung, Taiwan

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Background and aims: Decompressive craniectomy (DC) is thought to be one of the measures alleviating the impact of large hemisphere infarction with partial evidence. Limited data regarding the frequency and results of DC were reported from Asia.

Methods: Patients underwent DC due to large infarction from 2001 to 2007 were reviewed National Institute of Health Stroke Scale (NIHSS) at admission and serial Glasgow Coma Scale (GCS) at admission, before DC, 48 hours after DC, and at discharge were assessed retrospectively by one independent neurologist.

Results: 58 patients (right: 36, left: 21 and bilateral 1) were included. There were 22 (37.9%) women with mean age 64.3. The observation period was 415.1±529.8 days. Mortality rate was 32.8% (19/58) at discharge, 31.0% 30 days after stroke and 48.3% during observation period. Among survivors, NIHSS score was 21.3±6.6 at baseline (58), 21.9±7.6 at discharge (39) and 18.9±9.3 (30) at last observation. Among survivors, GCS was 10.7±3.0 at admission, 10.9±3.4 at discharge and 12.1±2.9 at last observation. Among survivors, mRS was 4.8±0.5 at admission, 4.9±0.4 at discharge and 4.6±0.8 at last observation. Among survivors, BI was 6.9±14.6 at admission, 7.7±11.8 at discharge and 19.0±26.6 at last observation. Among survivors, there was 23.3% (7/30) with MRS ≤4.

Conclusion: DC might be used in restricted incidence. Further well designed prospective trials are needed to prove the indication of DC.

Disclosure: Nothing to disclose

EP3051

An overlooked cause of coma - refeeding syndrome

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Background and aims: The refeeding syndrome is characterized by complex metabolic abnormalities, among them hypophosphatemia being the dominant one. The syndrome usually follows a period of fasting, has a heterogenous clinical presentation with a potentially fatal outcome if not recognized and treated accordingly.

Methods: We present the case of a 60-year-old male, suffering from chronic alcoholism, who 1 week prior to presentation in our unit was admitted in a detox centre. During his stay there he developed dysphagia, dysarthria, gait difficulty and eventually respiratory failure. He was then transferred to our unit, where he was intubated and mechanically ventilated. Computed tomography scan of the brain was suggestive of central pontine myelinolysis, but a subsequent magnetic resonance imaging study refuted this diagnosis. During his stay the patient displayed fluctuating levels of consciousness, ranging from 15 point on the Glasgow Coma Scale to 3 points within the same day, with corresponding fluctuation of the respiratory function (requiring reintubation and mechanical ventilation).

Results: On reevaluation of the history, it was revealed that he had precarious nutrition in the past months, and during the stay at the detox centre he consumed large quantities of food, with a high carbohydrate content. This fact combined with the history of alcoholism and lab results led to the diagnosis of refeeding syndrome. Parenteral phosphate supplementation was initiated, with gradual improvement of the clinical picture. He was discharged 1 week later with no neurological deficits.

Conclusion: Although often overlooked, refeeding syndrome should be considered as a differential diagnosis in rapidly developing muscular weakness and coma.

Disclosure: Nothing to disclose

EP3052

Double filtration plasmapheresis and therapeutic plasma exchange in severe neuroimmune diseases, a case series

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Background and aims: Therapeutic Plasma Exchange (TPE) and Double Filtration plasmapheresis (DFPP) are used in severe neurological diseases with autoimmune etiology representing an alternative to treatment with IV Immunoglobulin. Neurological disorders that plasmapheresis is accepted as first-line treatment are: Guillain Barre Syndrome, Myasthenia Gravis in severe crisis, Chronic Inflammatory Demyelinating polyneuropathy and fulminant forms of Wilson disease. Plasmapheresis is accepted as second-line therapy in: Lambert-Eaton Myasthenic Syndrome, Multiple Sclerosis relapsing-remitting form, also indicated in Acute Disseminated Encephalomyelitis and Optic Neuromyelitis unresponsive to high-dose corticosteroids. The aim of this study is to analyze indications, side effects and results of TPE and DFPP in severe neuroimmune diseases.

Methods: We present a retrospective study on 16 patients (6 Guillain-Barre Syndrome, 4 Myasthenia Gravis, 1 Chronic Inflammatory Demyelinating Polyneuropathy, 1 Multiple Sclerosis, 1 Necrotizing Myelitis, 1 Stiff-Man Syndrome, 1 West-Nile Encephalitis, 1 Optic Neuromyelitis), treated in our Intensive Care Unit with TPE and DFPP during 2013-2016.

Results: Thirteen patients had favorable evolution, only three died of sepsis developed during hospitalization. Side effects occurring during treatment were not severe (11 patients with hypocalcemia, 2 patients with hypotension, 3 patients with hypokaliemia, 4 patients with hyponatremia and 5 patients with sepsis) and did not require discontinuation of therapy.

Conclusion: This retrospective comparative study supports previous studies on the beneficial therapeutic effects and fast responsive of Plasmapheresis in neurological disabilities involving rapid progressive evolution.

Disclosure: Nothing to disclose

EP3053

Determining the factors affecting mortality of refractory status epilepticus in comparison with non-refractory status epilepticus - A retrospective study

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Background and aims: Afflicting up to 9-44% of all Status Epilepticus (SE) cases, Refractory Status Epilepticus (RSE) is an uncontrolled epileptic seizure activity unresponsive to first and second line SE therapy. Mortality of RSE is between 11-77%.

Aim: The aim of the study is to determine the factors affecting mortality of RSE in comparison with non-RSE.

Methods: 109 SE cases hospitalized in our neurological intensive care unit between 2011 and 2016 were included to this retrospective study. 52 were RSE and 57 were non-RSE. All clinical data about the clinical follow-up were emerged from the archive of the hospital. Factors which may cause mortality were categorized for statistical analysis.

Results: No significant relationship was found between mortality and refractoriness. Multivariate analysis revealed Intubation (OR=11.579, 95% G.A: 1.773-75.622, p=0.011), Glasgow Coma Score (GCS) at presentation (OR=0.149, 95% CI: 0.031-0.708, p=0.017) and hypotension (OR=11.579, 95% CI: 1.773-75.622, p=0.011) were the independent predictors of the mortality of all the SE population. GCS at presentation was the independent predictor of the mortality in RSE subgroup (OR=0.013, 95% CI: 0.001-0.319, p=0.008). No independent predictor of mortality was detected in non-RSE subgroup.

Conclusion: RSE is a serious clinical condition. Beside SE itself, mortality of SE is related with the complications of the interventions and the therapies which are applied during the follow-up. RSE cases could be more vulnerable in this term. Determining clinical features of RSE and defining predictors of mortality could be helpful for improving the outcome of RSE.

Disclosure: Nothing to disclose

EP3054

A retrospective study of psychiatric inpatients requiring intensive care unit admission

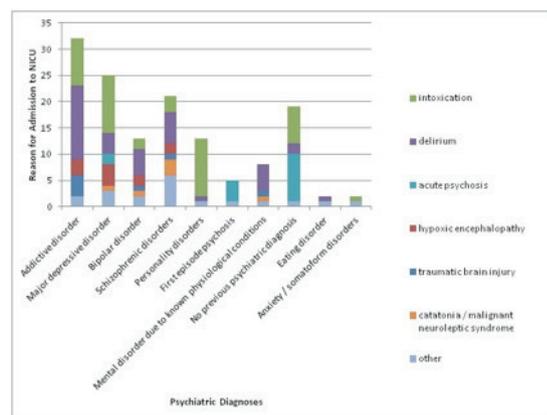
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Background and aims: Patients with mental and behavioral disorders may develop or inflict clinical conditions that require critical care. Here, we studied initial diagnoses, conditions necessitating critical care and mortality among psychiatric inpatients admitted to a neurological intensive care unit (NICU).

Methods: We performed a retrospective chart review of all patients hospitalized at the Department of Psychiatry Salzburg from 2000 to 2016 requiring admission to the NICU. We identified cases from the hospital documentation system and reviewed the NICU database for details of NICU interventions, course and outcome.

Results: We identified a total of 142 psychiatric inpatients which accounted for 2.2% of patients admitted to the NICU over the study period. The most common main psychiatric diagnoses (ICD-10) and reasons for admission are summarized in figure 1 and clinical details of the cohort are presented in table 1. Mean duration of stay was 6.5 days (range 1-55) and metabolic and hypoxic encephalopathies (62%) prevailed among patients with a stay beyond 10 days. Among the nine fatal cases (6%), four had been admitted after suicidal action (44%). The causes of death included cerebral hypoxia (n=6), multiple organ failure following intoxication, consequences of traumatic brain injury and respiratory insufficiency (n=1 each).



Reasons for ICU admission according to underlying psychiatric disorders

	Total n=142
Women, n (%)	72 (51)
Mean age, y (range)	46.7 (15-87)
Mean Glasgow Coma Scale on admission	9.6
Mean SAPS II score	25
Max. TISS 28 score	31
Mean Charlson Comorbidity Index	1.4
Mechanical ventilation, n (%)	38 (27)
Invasive hemodynamic monitoring, n (%)	129 (91)

Demographics and NICU parameters of psychiatric inpatients

Conclusion: Our study of psychiatric inpatients requiring critical care disclosed a broad range of reasons for NICU admission and underlying mental and behavioral disorders. The duration of ICU care was usually less than 10 days and need for mechanical ventilation was infrequent. Mortality was in part the consequence of suicidal action.

Disclosure: Nothing to disclose

Epilepsy 3

EP3055

Seizure semiology of temporal lobe epilepsy and outcome of anterior temporal lobectomy

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Background and aims: Seizure semiology is an indicator of the seizure onset zone, and can influence outcome of epilepsy surgery. We analysed the relationship between semiology of seizures during video-telemetry and outcomes following temporal lobectomy.

Methods: Adult patients undergoing anterior temporal lobectomy between 2008 and 2015 were included in the analysis. Demographic and clinical data were collected by review of patient records. Semiological features including presence and nature of aura, automatisms, and secondary generalised seizures were collected by review of video telemetry report. 12 month outcome was categorised based on Engel classification.

Results: 43 patients were included, with a median age of 41 years (21-63). 41 (95%) had MRI abnormalities, most commonly hippocampal sclerosis. Good (Engel class I) outcome was observed in 29 (69%) at 12 months. Seizure semiology was available for 42, of whom 32 (76%) reported an aura, most commonly epigastric (33%). Good outcome was seen in 23 (72%) of those who reported aura, and in 60% of those who did not ($p=0.69$). Automatisms were observed in 36 (87%) of patients, 25 (69%) of whom had good outcome, compared to 4 of 6 (67%) of those who did not have automatisms ($p=0.61$). Secondary generalised seizures occurred in 26 (62%), of whom 17 (65%) had a good outcome, compared to 12 of 16 (75%) who did not experience generalised seizures ($p=0.73$).

Conclusion: In this population of highly selected patients with lesional temporal lobe epilepsy, details of seizure semiology did not show significant association with outcomes from temporal lobectomy.

Disclosure: Nothing to disclose

EP3056

Idiopathic generalized epilepsy: valproic acid is still a main choice

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Background and aims: In the idiopathic generalized epilepsies (IGEs) there is no “underlying cause other than a possible hereditary predisposition”. Their onset is usually age-related and they constitute one-third of all epilepsies. Although few, several treatment options are now available. Our objective was to study antiepileptic drug (AED) use in IGEs in a specialized epilepsy unit where the use of new AEDs is favored.

Methods: We performed an audit searching for adult IGE patients seen in our unit from January/2016 to June/2016. Seizure types, epilepsy syndromes and definition of drug-resistant epilepsy were based on ILAE.

Results: We identified 72 patients (37 men/35 women) aged 18-85 years (mean=40±15.7). Mean age at epilepsy onset was 16 years. Epilepsy syndromes were: epilepsy with generalized tonic-clonic seizures alone(39%), juvenile myoclonic epilepsy(33%), childhood absence epilepsy(14%), juvenile absence epilepsy(11.2%), Jeavons syndrome (1.4%), unclassified IGE (1.4%). Seventeen patients (23.6%) were drug-resistant. Most common AEDs used were: valproic acid (VPA;58%), levetiracetam (36%), and lamotrigine (21%). Forty-six patients (62%) were seizure free (> 1 year), most on monotherapy (23 VPA, 9 levetiracetam, 7 other AEDs). Among patients treated with VPA, 23 were men (65% >600 mg/day) and 19 women (58% >600 mg/day). Most patients on VPA had failed previous AEDs (61% seizure-free).

Conclusion: In this series of IGE patients, VPA was the most widely used AEDs and achieved better seizure control than other AEDs. Most seizure-free patients were on VPA. Despite the advent of new AEDs, VPA is still a major drug needed to achieve seizure freedom in the IGEs.

Disclosure: Nothing to disclose

EP3057

Diagnostic usefulness and outcome of 24-48 hours inpatient Diagnostic Video-EEG monitoring for cases with recent onset paroxysmal events.

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Background and aims: Inpatient long-term video-EEG Monitoring for Epilepsy (LTME) is widely used for patients with paroxysmal events (epileptic and non epileptic). The diagnostic usefulness varies considerably depending on patient selection and referral category-diagnosis, seizure classification and presurgical evaluation. The purpose of this study was to assess diagnostic usefulness and management decisions of LTME in patients with recent onset seizures (within the previous 12 months) and inconclusive standard investigations before LTME.

Methods: We retrospectively reviewed data from 336 consecutive LTME-investigations over a 3-year referral period (January 2014-December 2016). There were 96 (57 males and 39 females) patients having inconclusive previous routine EEG and MRI studies. Patient ages ranged from 2 months to 74 years (0-14 yr: 48, 15-74yr: 48).

Results: Mean duration of LTME was 1,14 days. The events in question were recorded in 40/96 (41%). Interictal epileptiform abnormalities were detected in 52/96 (54%). In 24/96 (25%) studies there were no events and no interictal epileptiform abnormalities recorded. A diagnosis of epilepsy was established in 59 (62%), of Non-epileptic Events in 31 (32%), and was uncertain in 6 (6%). Considering all information, treatment and management modifications were implemented in 60 patients (63%).

Conclusion: We conclude that the diagnostic yield of even short-lasting LTME studies is still considerable in the particularly challenging category of patients with new-onset suspected epilepsy and inconclusive standard diagnostic work-up. Information thus gained may suggest management and treatment changes in as many as 60% of investigated cases.

Disclosure: Nothing to disclose

EP3058

The significance of focal EEG abnormalities in typical absence seizures – long term observations

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Background and aims: In last years it becomes more and more evident that focal EEG changes can be detected in patients with idiopathic generalized epilepsies. The aim of the study was to estimate the frequency of focal interictal EEG abnormalities in pediatric patients with absence seizures (ASs) and to identify their clinical, EEG and semiological correlates

Methods: Patients with typical absence seizures who were hospitalized or consulted at Dept. of Developmental Neurology between 2000 and 2015 were included in the study and followed prospectively. All patients underwent video-EEG monitoring at regular intervals. 149 patients who fulfilled criteria for typical absence seizures were included in the study.

Results: In 15% of patients we found interictal epileptiform discharges, and in 31% intermittent fronto-temporal slow waves. We found significant correlation between presence of interictal focal epileptiform discharges and long term prognosis, but did not find the correlation between worse prognosis and presence of fronto-temporal interictal slow wave activity. Interestingly, we did not find correlation between presence of focal abnormalities and worse performance in cognitive tests. The presence of focal EEG-changes were associated more frequently with presence of automatisms.

Conclusion: The value of focal interictal EEG abnormalities should not be overestimated according to prognosis and cognitive performance in children with typical absence seizures. The cautious EEG interpretation of focal changes in absence seizures is needed in order to prevent wrong diagnosis of focal epilepsy

Disclosure: Nothing to disclose

EP3059

Status epilepticus: causes and short-term outcome

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Background and aims: Status epilepticus (SE) is a severe expression of an acute brain insult or systemic disturbance which leads to excessive hyperexcitation of brain. This study aims to determine the most common causes and outcomes in patients hospitalized with SE in a regional academic hospital.

Methods: Over a 4-year period (Jan 1, 2012 to Dec 30, 2016) all patients older than 18 years with SE were included. The etiology, and outcome under Glasgow Outcome Scale (GOS) in 156 patients with SE (convulsive or non-convulsive), have been reviewed.

Results: The most common cause of SE was nonadherence with antiepileptic drugs (nAED) and this accounted in 67.3% of the patients with previous seizures and in 32.7% of all the patients. The other causes in our series were alcohol-withdrawal, cerebrovascular disease, cerebral tumors or trauma, infection, metabolic disorders, anoxia. SE was never the initial manifestation of further epilepsy. 92.3% of patients developed generalized tonic-clonic SE and only 3 (1.92%) patients presented with nonconvulsive SE. A poor GOS outcome of SE was correlated with cerebral infarction and increased age, low mortality rates were noted in alcohol and nAED etiologies.

Conclusion: Cerebrovascular disease and nAED were the most prominent causes of SE in this study. Low incidence of non-convulsive SE requires a better clinical evaluation and continuous EEG monitoring in suspected cases. GOS scores and etiology SE showed a better outcome in patients with nAED and unfavorable outcomes in elderly patients and those with acute brain injury such as stroke or cerebral anoxia.

Disclosure: Nothing to disclose

EP3060

Deep brain stimulation in adult-onset Rasmussen with disabling dystonia.

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Background and aims: Rasmussen's syndrome (RS) is a progressive inflammatory disease that involves one cerebral hemisphere and causes neurological deterioration and seizures. Rare cases of adults with RS and movement disorders have been described. We report an unusual case of adult RS with disabling focal dystonia and excellent response to contralateral pallidal stimulation.

Methods: The patient is a 40-year-old female suffering from focal perisylvian epilepsy since the age of 22. Seizures consisted of left hemiface paresthesias and tonic position of the left arm. Initially neurological examination and brain magnetic resonance imaging (MRI) were normal. At 38 she developed pain and abnormal dystonic posturing of the left leg two weeks after a motor vehicle accident. Lab tests for secondary dystonia were normal. MRI showed atrophy of the right cerebral hemisphere, predominantly in the insula and frontotemporal cortex, and decreased volume of right caudate nucleus. PET scan showed hypometabolism of right frontal and insular areas. Brain biopsy showed chronic encephalitis consistent with RS. Seizures remained under control with a combination of antiepileptic drugs but the dystonia increased in severity in spite of multiple immunomodulatory and antidystonic drugs. The patient was offered pallidal stimulation, which was performed eight years after onset of the dystonia.

Results: The abnormal movement has significantly improved and the patient is now able to stand and walk alone.

Conclusion: This case expands the clinical spectrum of movement disorders in adult RS. To our knowledge, this is the first case of disabling dystonia in adult RS treated with GPi-DBS, with good outcome.

Disclosure: Nothing to disclose

EP3061

Unusual ictal features in temporal lobe epilepsy

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Background and aims: Temporal Lobe Epilepsy (TLE) is the commonest form of location-related epilepsy. The ictal manifestations of TLE are typically quite stereotyped - it usually presents with recurrent complex focal seizures, often preceded by vegetative auras. However, unusual semiologic features have been described, rendering the localization of the epileptic discharge less straightforward.

Results: Case reports: Four drug-resistant epileptic patients (aged between 15 and 42 years) with uncommon seizure descriptions completed Video-Electroencephalography monitoring (VEEG) for diagnostic and pre-surgical evaluation purposes. All had seizures during the VEEG, and detailed video analysis was performed. Patient One had two seizures with hypermotor bilateral leg movements and left-hand dystonic posturing. Patient Two had two seizures with echolalia and echopraxia, and late right-hand dystonic posturing. Patient Three had four abrupt-onset hypermotor seizures and one complex focal seizure. Patient Four had eleven seizures with urinary urge and upper limbs choreiform movements. Ictal electroencephalogram was compatible with temporal lobe origin. All patients had lesions located in the temporal lobe; two of them underwent anterior temporal lobectomy, both with favorable outcomes. The remaining patients are currently undertaking further pre-surgical investigation.

Conclusion: Clinical semiology remains the starting point for the diagnosis and classification of epilepsy. It is equally invaluable for the determination of the seizure onset zone in surgical candidates. Nonetheless, although many semiologic features have high localizing value, each of them has also some potential to falsely localize. We present four patients whose ictal manifestations were unusual for TLE, reinforcing the importance of correlating clinical with EEG and imaging findings.

Disclosure: Nothing to disclose

EP3062

Experience with the use of Perampanel (PER) as first add-on in routine clinical practice. A multicenter study in Spain

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Background and aims: Some studies in clinical experience with Perampanel (PER) suggest that patients taking fewer prior AEDs had a more favourable clinical response, however there are no series focused exclusively early use. Based on these data, we aimed to evaluate the use of PER as first add-on treatment in patients with focal epilepsy and idiopathic generalized epilepsy (IGE).

Methods: We selected retrospectively with PER as first add-on from six Spanish centers. We collected demographics, type of epilepsy, concomitant treatment and we analysed the improvement of seizure frequency, the presence of adverse events (AEs) and the retention rate at 3 and 6 months.

Results: 49 patients were evaluated. Mean age: 44.8 (17-76) years old. 31(63.3%) were male. 18(36.7%) were diagnosed as symptomatic focal epilepsy, 17(34.7%) as cryptogenic focal epilepsy, 9(18.4%) as IGE and 5 (10.2%) as undefined epilepsy. At 3 months follow-up: 38 (77.8%) showed efficacy, including 15 (30.6%) seizure-free and 32 (65.3%) with a seizure reduction>50%. 17 (34.7%) had AEs (5 fatigue/somnolence, 4 irritability, 8 dizziness). The median dose was 4 mg. The retention rate was 77.6%. At 6 months (n=37), PER was effective in 33 (89.2%) remaining 14 (37.8% seizure-free and 29 (59.2%) and with a reduction>50%. 11(29.7%) had AEs (3 fatigue/somnolence, 2 irritability, 2 dizziness, 1 anosmia). Retention rate was 89.2%. The median dose was 6 mg.

Conclusion: In clinical practice, the adjunctive treatment with PER as first-add may lead to an improvement in seizures frequency. It seems a well tolerated drug as add-on with a low rate of AEs.

Disclosure: Nothing to disclose

EP3063

Cluster seizures – what really counts?

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Background and aims: Cluster seizures (CS) are commonly observed among patients with drug resistant epilepsy or acute brain damage. However despite its occurrence, there was not indicated precisely prognostic factors or tools. The aim of this study was to determine a risk factors for poor outcome.

Methods: We retrospectively reviewed 200 patients with CS in a 5-year period and considered all potential predictors of poor outcome for patients with continuous seizures. Unfavorable outcome was defined as a modified Rankin Score ≥ 5 . A univariate and multivariate analysis was used to determine the predictors.

Results: Mortality counted 20 cases (10%) of patients on analyzed cohort. The risk factors of death in univariate analysis included age ($p < 0.001$), history of drug resistant epilepsy ($p = 0.03$), acute ($p = 0.005$) and idiopathic etiology ($p = 0.017$), level of consciousness ($p < 0.001$), seizure type (0.05) and seizure progressing to status epilepticus ($p < 0.001$). Thereafter, independent predictors were defined as age (OR=0.1; years), acute etiology (OR=4.1), level of consciousness (OR=3.0) and seizure type (OR=3.2).

Conclusion: CS patients are frequently overlooked in literature, however represent important population due to its mortality rates. Therefore indicated predictive factors should be considered within diagnostic/treatment procedures.

Disclosure: Nothing to disclose

EP3064

Simple neurovascular reactivity in patients with idiopathic generalized epilepsy

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Background and aims: Simple neurovascular activation by transcranial Doppler (TCD) is not presented to date in drug responsive patients with idiopathic generalised epilepsy. The objective of this study is to assess the neurovascular activation to simple visual stimulation of patients with idiopathic generalised epilepsy during interictal period.

Methods: Thirty-four patients with idiopathic generalised epilepsy at least ten days later after last epileptic attack and 14 healthy subjects were screened for this study in our Neurosonology Laboratory. We performed trans-temporal TCD recordings from the P2-segments of both posterior cerebral arteries (PCA) simultaneously during simple visual stimulation. The individual reactivity was defined as a relative increase of the blood flow velocities as a percentage change of the baseline values.

Results: None of the patients has an epileptic focus on the brain documented by the MRI, nor EEG. The Doppler data of the patients and healthy subjects showed non-significant side difference, and therefore, were analysed 68 vessels in patients and 28 vessels in controls. The blood flow velocity during stimulation and simple visual reactivity were slightly lower in the patients (42.5 cm/s and 25.6%, respectively) from those of the controls (44.7 cm/s and 29.4%, respectively) ($p = 0.3$ and $p = 0.1$, respectively).

Conclusion: Our study showed the temporal and occipital region of brain perfused by PCA of the patients with idiopathic generalised epilepsy have normoactive neurones during the interictal period when comparing with the healthy subjects, or under appropriate antiepileptic treatment, neuronal hyperactivation could be successfully inhibited at least too weak stimulus likewise simple visual stimulation.

Disclosure: Nothing to disclose

EP3065

Long-term follow-up of five cases with late-onset Rasmussen encephalitis in University Hospital Bratislava, Slovakia.

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Background and aims: RE is a rare disease. Most cases start in children under 10 years, about 10% of cases in adolescence or early adulthood. These cases are typical with slower course of disease.

Methods: In University Hospital in Bratislava, Slovakia, we follow five patients with late onset of RE. 2/5 are women. Patients are 23 to 59 ys old, median 35ys. The patients suffered their first epileptic seizure between 6 and 30 ys of age, median 18. All 5 pts started with motor seizures. They suffered first epileptic state between 19-46ys, median 28y. Two of them presented with epilepsy partialis continua (EPC). Atrophy of the brain was verified in 4 of them. Two out of them presented with anti-GAD antibodies, three of them without detectable antibodies in the sera.

Results: All patients were treated with immunomodifying therapy - intravenous immunoglobulins, plasmaexchange, azathioprin, rituximab, corticosteroids in individualized regimens. In 4/5 the neurological deficit is still mild, with mild cognitive decline, but the epilepsy is the main problem. The diagnosis of RE was delayed 1-16 years from the first epileptic seizures, median 4 years. The brain hemiatrophy was verified in patients 4-14 years after first epileptic seizure.

Conclusion: Late onset RE is extremely rare. Due to its slower course, delay between first epileptic seizures and first epileptic state, it might be not recognized for many years. Immunotherapy of late onset RE is the treatment of the first choice. The hemispherectomy could be postponed.

Disclosure: Nothing to disclose

EP3066

Epilepsia Partialis Continua in Creutzfeldt Jacob DiseaseS. Ufuk Ersoy¹, G. Kutlu²¹Nicosia, Cyprus, ²Ankara, Turkey

Background and aims: Creutzfeldt-Jacob Disease is a progressive, degenerative disease of the central nervous system. It occurs as a result of prion protein deposition. Progressive dementia, myoclonus, cerebellar, pyramidal and extrapyramidal symptoms are characteristic for this disease.

Methods: 57 years old male patient applied to emergency service with symptoms of dementia, bizarre behaviours and continuous involuntary contractions on the left arm. He was having calculation and memory problems for the last six months. And for the last four months he started to show psychiatric symptoms. At the same time involuntary movements on his left arm were seen. At another health center, after a normal brain MRI scan he was put on olanzapin and oxcarbazepine. However his symptoms proceeded. He began to be very agitated and the involuntary contractions became worse. So his family brought him to emergency service. There he was diagnosed as encephalitis and interned to infection diseases department. However, his cerebrospinal fluid cultures did not show any evidence of infection. Later he was consulted to our neurology department because of these non-stop contractions on his left arm. His brain MRI scan showed bilateral basal ganglion intensity increase. There were PLEDs in his EEG. And 14.3.3 protein was positive in his cerebrospinal fluid. With these findings he was diagnosed as Creutzfeldt-Jacob disease with epilepsy partialis continua.

Results: In the literature, there are very few Creutzfeldt-Jacob disease cases that have epilepsy partialis continua.

Conclusion: We present this case to underline that, at early stages of Creutzfeldt-Jacob disease focal motor seizures can be seen.

Disclosure: Nothing to disclose

EP3067

One-year experience with perampanel – focus on psychiatric adverse effects

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Background and aims: Perampanel (PER) is a new antiepileptic drug (AED) licensed as an adjunctive treatment of partial-onset seizures and primary generalized tonic-clonic seizures. In the Czech Republic, PER is available since June 2015. We performed a retrospective analysis of one-year experience with PER in 87 patients treated in tertiary epilepsy centre.

Methods: The demographic and clinical data of the patients were collected by review of medical records in the hospital database. Type of epilepsy, seizure type, used PER dosage, concomitant AEDs, adverse effects and reasons for withdrawal were analyzed.

Results: Out of 87 patients with drug-refractory epilepsy (49 females, median age 35, range 18-66), 78 had focal epilepsy, six generalized and four unclassified epilepsy. Apart from PER they were treated with median of three AEDs (range 1-5). At least transient positive effect was reported in 35 patients (40%). 35 patients (40%) were withdrawn from PER, 21 (60%) due to adverse effects, three because of no efficacy and 11 (31%) due to combination of both. Adverse effects at some point were reported by 47 patients (54%), most common were fatigue (30%), dizziness (14%) and instability (10%). Psychiatric adverse effects included change in behavior (11%), aggression (6%), lacrimosity (3%), one patient with depression and suicidal ideation and one case of psychosis. Psychiatric adverse effects led to withdrawal of PER in ten out of 11 patients.

Conclusion: PER showed at least transient positive clinical effect in 40% of patients. Psychiatric adverse effects were observed in 13% of patients and led to withdrawal of PER in most cases.

Disclosure: Nothing to disclose

EP3068

Cancelled

Headache and pain 3

EP3069

Measurement of the cerebrospinal fluid pressure in spontaneous intracranial hypotension syndrome

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Background and aims: The intracranial hypotension syndrome (IHS) is an entity whose main symptom is an intense headache that occurs or worsens with upright posture. The diagnosis is usually confirmed by demonstrating low cerebrospinal fluid (CSF) opening pressure, also supported by characteristic image findings in brain magnetic resonance (MR). To discuss whether lumbar puncture is indispensable or not, we describe a clinical case.

Methods: Woman of 27 years old with 20 days of spontaneous orthostatic headache, exacerbated by Valsalva maneuver, and relieved by recumbency, associating nausea and vomits. There were no relevant findings in physical and neurological exam, ophthalmoscopy or brain computed tomography (CT).

Results: Brain MR imaging detected descent of the hypothalamus, the optic chiasma and the cerebellar tonsil, important compression of the pons, and diffuse pachymeningeal enhancement. It also demonstrated a spinal meningeal diverticulum in D8-D9 that was the origin of the CSF leakage. After 33 days of postural treatment in Trendelenburg and caffeine, the patient presented spontaneous recovery. The diverticulum disappeared in the latest images.

Conclusion: Spontaneous IHS with no signs of complication usually respond to conservative treatment. The fact that the lumbar puncture it is not a harmless test, but it can make the headache worse, contribute to cerebral herniation or even create a new fistula, made us consider if it is essential to perform it when the whole symptomatology and the brain MR images are compatible with the diagnosis. It is a good argument to start with conservative measures, not making any more invasive tests if they are effective.

Disclosure: Nothing to disclose

EP3070

Early onset of efficacy with erenumab in a phase 2 clinical trial of subjects with chronic migraine

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Background and aims: Erenumab 70mg and 140mg reduced monthly migraine days at all time points assessed (weeks 4, 8, 12) in a phase 2 clinical trial of chronic migraine (NCT02066415). Here, we evaluated efficacy prior to week 4.

Methods: Post-hoc analyses evaluated achievement of $\geq 50\%$ reduction in weekly migraine days (WMDs) and change from baseline in WMDs. P-values for these endpoints are based on odds ratios or mean differences from placebo, not adjusted for multiplicity. Also, to evaluate trends, a linear model was fitted to observed daily migraine days for days 1-7 (week 1), and pairwise comparisons of the slopes and moving averages were evaluated and overlaid with observed data.

Results: Both erenumab dose groups had a greater proportion of patients achieving $\geq 50\%$ reduction in WMDs by week 1; 26% for both doses vs 16% placebo ($p \leq 0.011$), increasing to 31%, 41%, and 21% in the 70mg, 140mg, and placebo groups, respectively, at week 2 ($p \leq 0.011$). At weeks 1-4, reductions from baseline in WMDs were observed with both doses vs placebo ($p = 0.047$ at week 1 for 70mg and $p \leq 0.002$ at weeks 2-4 for both doses). Moreover, 7-day moving averages of observed data showed that each treatment arm differed from placebo within the first several days. On pairwise comparisons, slopes for 140mg differed from placebo by day 4 ($p = 0.03$). By day 6, both doses differed from placebo ($p \leq 0.03$), but differences between doses were not detected ($p = 0.86$).

Conclusion: Erenumab showed early onset of efficacy, with separation from placebo within the first week.

Disclosure: Funding for this study was provided by Amgen Inc.

EP3071

Eagle Syndrome: An uncommon mimic of glossopharyngeal neuralgia (GN)J. Rodríguez-Vico¹, M. Oses¹, M. Machío²¹Neurology, Fundación Jiménez Díaz University Hospital, Madrid, Spain, ²Neurology, FJD, Madrid, Spain

Background and aims: Eagle syndrome (ES) is defined as a symptomatic elongation of the styloid process or mineralization of the stylohyoid ligament. Classic ES, is seen after tonsillectomy or minor trauma. Pain is often felt on the angle of the mandible and may radiate to the ipsilateral ear. Patients also complain of dysphagia, tinnitus, sensation of foreign body in the throat and otalgia. Impingement of close cranial nerves is thought to cause the pain. Diagnosis is based on clinical signs, digital palpation of styloid process in the tonsillar fossa, radiological findings, and Lidocaine infiltration test. Three dimensional CT is considered the Gold standard for the diagnosis of ES. Differential diagnosis includes GN. The negativity of first examination and no reaction to infiltration of corticosteroid in the hyoid area, made the diagnosis delayed.

Methods: Clinical case report.

Results: We report a 55-year-old woman who presented with a constant pain in the right side of the face close to the angle of mandible and sensation of foreign body in the throat on swallowing. Physical examination revealed no exacerbation of the pain by palpation of the right tonsillar fossa. Carbamacepine and Eslicarbacepine were useless. Corticosteroid infiltration of the hyoid process was negative. Computed tomography (CT) of the neck with three-dimensional reconstruction showed elongation of the right styloid process. Surgery was proposed.

Conclusion: ES may be confused with GN, like in our case. It's a rare condition but not uncommon. We should keep in mind when managing refractory GN.

Disclosure: Nothing to disclose

EP3072

Brain white matter and infarct-like lesions in primary headache: an Italian single centre studyM. Romoli¹, S. Caproni¹, G. Bellavita¹, I. Corbelli¹, A. Verzina¹, L. Bernetti¹, P. Eusebi², P. Sarchielli¹, P. Calabresi¹¹Neurology Clinic, University Hospital of Perugia, Perugia, Italy, ²Department of Public Health, University of Perugia, Perugia, Italy

Background and aims: White matter lesions (WMLs) and infarct-like lesions (ILLs) are frequently detected with brain imaging techniques in patients suffering from headache, especially among migraineurs. The aim of the study was to evaluate the prevalence of WMLs and ILLs in an Italian cohort of patients with primary headache.

Methods: This retrospective study collected data of patients admitted at the Headache Center of Perugia in 2012, undergoing MRI scan and diagnosed with a primary headache disorder. Patients were excluded in case of (i) secondary headache, (ii) major comorbidities and (iii) conditions associated with brain hyperintensities without migraine. Headache was classified following the 2nd ICHD revision. Brain MRI were performed on 1.5 T magnet device, with ILLs and WMLs being rated according to reported paradigms (Fig 1).

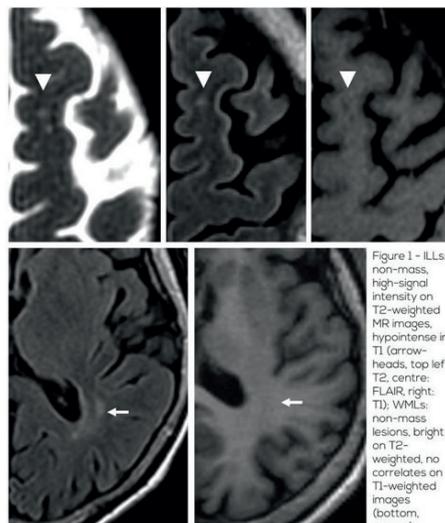


Figure 1. Infarct like lesions (ILLs) and white matter lesions (WMLs) appearance on brain MRI.

Results: Overall, 824 patients were enrolled: 721 (87.5%) had migraine without aura (M), 69 (8.3%) had migraine with aura (MA), 27 (3.2%) had medication overuse headache (MOH), 7 (0.8%) had cluster headache (CH). WMLs prevalence was higher in MOH compared to other groups, while ILLs were more frequent in CH (Table 1) ($p < .05$). M and MA had similar prevalence of WMLs and ILLs, though M was more associated with both.

	M	MA	CH	MOH
Number	721	69	7	27
Female	569	49	2	25
	79%	71%	29%	93%
Mean age	36.2	36.7	35.5	43.3
WMLs	77	6	1	7
	10.7%*	8.7%*	14.3%*	25.9%*
ILLs	82	6	3	4
	11.4%*	8.7%*	42.9%*	14.8%*

* p<.05

Abbreviations: CH=cluster headache; ILL=infarct-like lesions; M=migraine without aura; MA=migraine with aura; MOH=medication overuse headache; WMLs=white matter lesions.

Results and demographic data of the study cohort

Conclusion: Our data confirm the association between WMLs and ILLs with primary headache disorders. MOH was associated with the highest prevalence of WMLs, and had increased prevalence of ILLs compared to M and MA. Population-based assessment should continue in order to better define prevalence and implications of WMLs and ILLs in headache disorders in the Italian population.

Disclosure: Nothing to disclose

EP3073

Variation of the spontaneous blink rate (SBR) in light and dark: comparison between migraine patients and healthy subjects

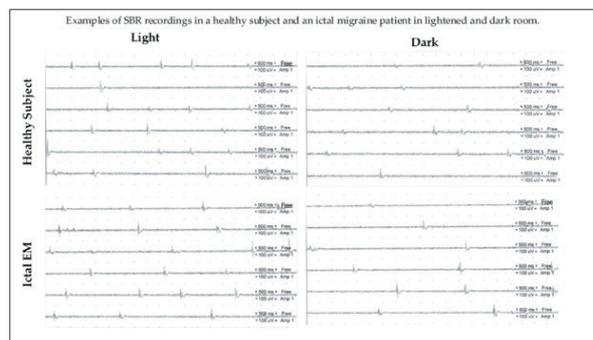
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Background and aims: The spontaneous blink rate (SBR) is strongly modulated by dopamine (Karson et al., 1982) and by the occipital cortex (Karson et al., 1990) both of which also play a role in migraine pathophysiology (Charbit et al., 2010). Photophobia is a phenotypic hallmark of migraine both during and between attacks. We searched therefore whether the SBR could be increased in migraineurs because of their sensitivity to light.

Methods: We enrolled a total of 38 subjects: 7 healthy subjects (HS), 19 interictal episodic migraineurs (EM) and 10 ictal EM without prophylactic treatment. The SBR was measured in a lit room at a luminance intensity of 145 Lux or in almost total darkness, 12 Lux, using 2 electrodes placed on the orbicularis muscle of the right eye.

Results: We found no difference between groups during lightened sessions. By contrast, in the dark the SBR was reduced in HS and in ictal EM, but not in interictal EM (p=0.05). The percentage SBR change between light and dark was -36.71±22% in HS, -18.7±34.74% in ictal EM and 1.9±43.98% [SD] in interictal EM. This change was significant in HS (p=0.017).



Conclusion: We show that in migraine patients between attacks the SBR is not decreased in the dark like in healthy subjects or migraineurs during an attack. This could be due to an abnormal interictal control by dopamine and/or the occipital cortex that normalizes during the attack.

Disclosure: Acknowledgement: this study was supported by FP7-EUROHEADPAIN no. 602633

EP3074

Differential sensitivity to blue or red flash light at 5 or 20 Hz in healthy subjects and migraine patients.

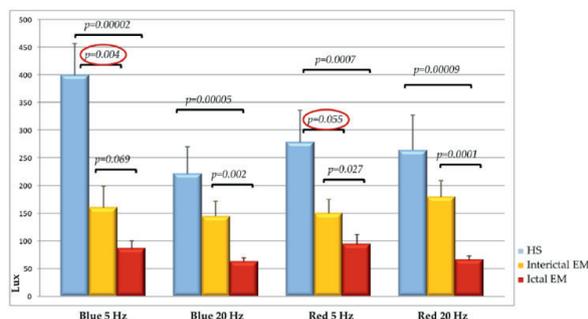
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Background and aims: Migraine patients are known to be sensitive to light during an attack, but also interictally. Our purpose was to determine whether flash light sensitivity differs between colours and stimulation frequencies in healthy subjects (HS) and episodic migraine patients (EM) during and between attacks.

Methods: We enrolled a total of 36 subjects: 7 HS, 10 interictal EM and 19 ictal EM. Stimulation intensity increased by steps of 50 Lux, beginning at 50 Lux. We tested in random chronological order 4 dynamic sequences: blue (~470 nm) at 5 Hz and 20 Hz, red (~720 nm) at 5 Hz and 20 Hz. The subjects were asked to request interruption of the stimulation as soon as they perceived it as uncomfortable.

Results: Compared to HS, interictal EM patients were more light-sensitive to the 5 Hz blue sequence ($p=0.004$) while ictal EM patients were more sensitive to the 5 Hz blue stimulation ($p=0.00002$), the 20 Hz blue ($p=0.00005$), the 5 Hz red ($p=0.0007$) and the 20 Hz red ($p=0.00009$).

EM patients reported a greater sensitivity during than outside of an attack for the 20 Hz blue sequence ($p=0.002$), 5 Hz blue ($p=0.027$) and 20 Hz red ($p=0.00019$).



Conclusion: Compared to healthy subjects, migraineurs are more sensitive to blue light and low stimulation rates, suggesting that these parameters may not be suitable for therapeutic purposes and that the melanospin ipRGC pathway is involved. The study also confirms that patients are more sensitive to light during attacks whatever the light parameters are.

Disclosure: Acknowledgement: this study was supported by FP7-EUROHEADPAIN no. 602633

EP3075

Management and treatment challenges for patients with chronic migraine, application of OnabotulinumtoxinA: early results of 70 patients

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Background and aims: Chronic migraine is a distinct subtype of Chronic Daily Headache. The impact of chronic migraine can be very disabling. Many of the therapies prescribed for chronic migraine are the same as those prescribed for episodic migraine. However, treatment still remains to be a challenge and application of OnabotulinumtoxinA might prove to be beneficial for this patient group. In this retrospective study, the effects of OnabotulinumtoxinA for the prophylactic treatment of headaches in chronic migraine patients were assessed.

Methods: Headache patients who were followed up between 2014 and 2016 at a headache unit were retrospectively assessed and patients with the diagnosis of chronic migraine who were refractory to medical treatments and were treated with OnabotulinumtoxinA were involved into the study. Patient records were reviewed and neurological exams, the frequency and severity of headache, the need for symptomatic treatment and effects on quality of life were all evaluated.

Results: 70 patients (52 females, 67.5%) were enrolled into the study. All patients had previous history of multiple drugs but remained symptomatic. Patients were also evaluated before OnabotulinumtoxinA as well as 1. and 3. month after application. OnabotulinumtoxinA was easily tolerated with no serious side effects.

Conclusion: Chronic migraine is a debilitating disease effecting the quality of life of sufferers. For prophylaxis against chronic migraine, literature suggests that the average benefit for OnabotulinumtoxinA seems to be statistically significant. OnabotulinumtoxinA seems to be a safe and tolerable treatment method for chronic migraine.

Disclosure: Nothing to disclose

EP3076

Cancelled

EP3077

Repetitive TMS over the primary motor cortex for prophylactic treatment of migraine

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Background and aims: Patients with chronic migraine (CM) have worse quality of life, increased headache - related burden and worse psychiatric and medical comorbidities in comparison with patients with episodic migraine. We investigated the safety and efficacy of high frequency (HF) repetitive transcranial magnetic stimulation (rTMS) in 40 patients with CM.

Methods: All the patients were diagnosed with chronic migraine according to the criteria of IHS classification ICHD - 3 beta. The stimulation protocol was HF rTMS (15 Hz, 70% of the motor threshold, 1200 pulses/session) over the primary motor cortex (M1) for 5 consecutive sessions. The patients kept a headache diary and were evaluated 30 days after the last session. We studied the change in the frequency of headache, symptomatic medication use, headache intensity measured with visual analogue scale and the result on Headache Impact Test - 6 (HIT - 6). For statistical analysis we used Wilcoxon Signed Rank Test.

Results: In 77% of the patients we observed reduction of $\geq 50\%$ of the number of migraine days; 78% had reduction of ≥ 50 of the number of days with acute medication use; 82% had reduction of migraine headache intensity; 85% had reduction of the overall headache intensity per month and 79% had clinically significant improvement in the HIT - 6 score. There were no serious adverse events.

Conclusion: Repetitive HF rTMS over M1 is safe and shows effectiveness for CM treatment.

Disclosure: Nothing to disclose

EP3078

Primary headaches in Armenia: An underestimated medical problem

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Background and aims: According to data of WHO Primary Headaches (PH) have both substantial burden on patients and their family life and consist serious social-economic problem. Aim of our study was investigation of prevalence of different types of PH (tension type, migraine, cluster and other cephalalgias) in patients under neurological control.

Methods: 150 (113 women/ 37 men) patients with PH (migraine, tension type ad trigemino-autonomic cephalgia correspondingly) underwent special investigations including questionnaires, created correspondingly to diagnostic criteria and recommendations of International Headache Society, HIT-6, SF -36 questionnaires. Age of participants was 42 ± 16 years.

Results: Data analysis revealed that 90 patients (60%) has migraine, 47 (31%) tension type, 7 (5%) cluster headache, 4 (3%) paroxysmal hemicrania, 1 (1%) hemicrania continua and 1 (1%) SUNCT -syndrom. Main part of patients - 91 patient (60%) was adressed to doctors (68 from which adressed to neurologists) previously and were misdiagnosed with other conditions. Therefore, previous treatment failed to heal the headaches.

Conclusion: Our data shows some different distribution of PH types than international, in our opinion those are patients from the selected treated group, but not from general population. We conclude that is serious misdiagnosing and low awareness of all types of PH by many doctors. We need improvement in both education of medical specialists and patients, to improve both awareness and management of PH in the country.

Disclosure: Nothing to disclose

EP3079

Burden of migraine in the 5EU from the patient perspective: A cross-sectional analysis of National Health and Wellness Survey (NHWS) data

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Background and aims: Migraine is one of the most disabling neurological conditions worldwide. The purpose of this study was to characterize the incremental burden of migraine on quality of life (QoL), productivity, and healthcare resource utilization (HRU) by the frequency of migraine in adults using European data from the National Health and Wellness Survey (NHWS), a self-administered, internet-based questionnaire.

Methods: A retrospective, cross-sectional analysis of responses from the 2016 NHWS was performed using data from the France, Germany, Italy, Spain, and UK (5EU). Adult NHWS respondents with a self-reported migraine diagnosis who completed the migraine module were matched by propensity scores to those without migraines (controls) using sociodemographic characteristics. Outcomes of interest analyzed were from EQ-5D, SF-36v2, HRU and the Work Productivity and Activity Impairment (WPAI-GH) questionnaires. Migraine respondents were stratified by frequency of migraines (headache days/month): 4-7 episodic migraine (EM), 8-14 EM, and chronic migraine (≥15; CM). Independent sample t-tests were used to determine significant differences between controls and the frequency of migraine groups.

Results: Results from the propensity score matched analysis demonstrated that migraineurs reported statistically significant lower QoL and higher HRU as compared to their matched controls. Impairment while at work and total activity impairment was statistically significant higher among all migraineurs compared to matched controls (Table 1).

	Non-migraine controls (a) (N=218)	Migraine (b) (N=218)	4-7 EM (c) (N=106)	8-14 EM (d) (N=49)	CM (e) (N=63)
SF6 Utility Score (mean, SD)	0.71 (0.14) _a	0.62 (0.12) _b	0.64 (0.13) _b	0.62 (0.12) _b	0.57 (0.11) _b
EQ-5D utility index (mean, SD)	0.81 (0.21) _a	0.68 (0.28) _b	0.74 (0.25) _b	0.70 (0.28) _b	0.56 (0.27) _b
SF-36v2 MCS (mean, SD)	44.82 (11.39) _a	37.69 (11.72) _b	39.64 (11.27) _b	36.34 (11.09) _b	35.47 (12.55) _b
SF-36v2 PCS (mean, SD)	50.51 (9.54) _a	46.00 (9.81) _b	47.89 (9.89) _b	47.28 (7.53) _b	41.81 (10.09) _b
Health status (EQ-5D VAS, mean, SD)	70.99 (24.11) _a	60.06 (24.14) _b	64.54 (22.63) _b	62.98 (24.93) _b	50.24 (23.52) _b
*Absenteeism (% work time missed, mean, SD)	9.46 (24.61) _a	14.43 (27.17) _b	7.98 (19.57) _b	22.19 (34.00) _b	19.65 (30.36) _b
*Presenteeism (% impairment while at work, mean SD)	20.97 (25.77) _a	35.52 (29.22) _b	29.38 (29.70) _b	33.79 (27.44) _b	49.38 (25.77) _b
*Overall work impairment (% overall impairment related to work, mean, SD)	23.27 (28.24) _a	38.70 (31.59) _b	31.09 (30.82) _b	39.10 (32.26) _b	53.56 (27.81) _b
Total activity impairment (% mean, SD)	27.75 (28.48) _a	44.17 (30.25) _b	37.74 (31.12) _b	42.86 (30.89) _b	56.03 (25.13) _b
Number of healthcare provider visits in the past 6 months (mean, SD)	5.13 (6.86) _a	8.48 (10.89) _b	7.25 (7.29) _b	7.06 (7.64) _b	11.65 (16.30) _b

Table 1 Results on domains of health status, QOL and work productivity in migraine subgroups after propensity score matched analysis with non-migraine controls across 5EU

Conclusion: Migraine is a chronic disorder negatively affecting multiple domains of individuals' lives. This study demonstrated that there is a statistically significant incremental burden due to migraine on QoL, HRU and work productivity amongst the migraineurs in comparison to matched controls.

Disclosure: This study was sponsored by Novartis Pharma AG, Basel, Switzerland.

EP3080

A descriptive analysis of the burden of migraine based on self-reported migraine diary data using the Migraine Buddy application in Europe

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Background and aims: Migraine is a neurological disorder that can cause severe disabling pain. The purpose of the study was to describe the burden of migraine on health-related quality of life (HRQOL) as perceived by individuals suffering from migraine in the real world using a self-reported mobile application.

Methods: A retrospective, cross-sectional analysis was conducted using data captured through the Migraine-Buddy© smartphone application from adult, self-diagnosed migraineurs in several European countries including the UK, France, and Spain. Data was analyzed for the most recent 28-day period reported by migraineurs during the study period (June 2015-July 2016). Migraine respondents (n=3900) were randomly selected based on data completeness (fill rates >70%) and stratified by migraine headache days/month: 4-7 episodic migraine (EM) (n=1500), 8-14EM (n=1500), and chronic migraine (≥15; CM) (n=900). Descriptive analysis was performed.

Results: More than 95% of 3900 self-reported migraineurs reported that migraine negatively impacted their daily activities in at least one migraine attack. Attacks affected 50.5% (184.4 days/year), 26.9% (98 days/year) and 14.5% (53 days/year) of their calendar year among CM, 8-14EM, and 4-7EM groups, respectively. On average, 44.8% CM, 40.9% 8-14EM and 34.7% of 4-7EM sufferers respectively reported anxiety and/or depression symptoms during migraine attacks. Social or home activities, productivity, or sleep were highly impacted in migraineurs (Table 1). Triptans (68%), opioids (46%) and nonsteroidal anti-inflammatory drugs (45%) were self-reported as the most common medicines used by migraineurs.

Type of activity	CM (N=900)		8-14EM (N=1500)		4-7EM (N=1500)	
	n	%	n	%	n	%
Home activities	520	57.8%	985	65.7%	933	62.2%
Productivity	590	65.6%	993	66.2%	841	56.1%
Sleep	470	52.2%	827	55.1%	676	45.1%
Social activities	553	61.4%	882	58.8%	736	49.1%
Others	268	29.8%	298	19.9%	204	13.6%

Impact of migraine on daily activities (Number and proportion of patients by subgroup reporting impact from migraine on daily activities is shown)

Conclusion: This study highlights the high burden of migraine on HRQOL and overall well-being of individuals suffering from migraines.

Disclosure: This study was sponsored by Novartis Pharma AG, Basel, Switzerland.

EP3081

Understanding the impact of migraine on work productivity using self-reported migraine diary data using the Migraine Buddy application in Europe

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Background and aims: The purpose of the study was to evaluate the impact of migraine on work productivity as perceived by individuals suffering from migraine in the real world using a self-reported smartphone application called Migraine-Buddy©.

Methods: A retrospective, cross-sectional analysis was conducted using data captured through Migraine-Buddy© from adult, self-diagnosed migraineurs in 17 European countries. Data was analyzed for the most recent 28-day period reported by migraineurs during the study period June 2015-July 2016. Data from chronic migraine (CM: ≥ 15 headache days/month, N=900), 4-7 episodic migraine (EM) (n=1500) and 8-14 EM (n=1500) individuals were randomly selected based on data completeness (fill rates >70%). Descriptive analysis was performed.

Results: A total of 10,347, 11,301 and 6,504 migraine records were retrieved from CM, 8-14 EM and 4-7 EM individuals, respectively corresponding to a total of 16,815, 14,398, and 7,693 migraine days. Among employed migraineurs (n=2,722) who declared 'work' either as their migraine location or in 'affected activities' at least once, an average of 61.7, 31.6 and 18.4 work days missed per year were reported by CM (n=679), 8-14 EM (n=1084) and 4-7 EM (n=959) sufferers, respectively. The most commonly reported triggers of absenteeism-related migraines were psychological (38%), sleep (34%), nutrition (25%) and/or menstruation (23%). Employed sufferers reporting absenteeism recorded symptoms relating to pain/body, mood/cognition disturbances, environmental handicap and depression among others (Table 1).

Symptoms	CM (N=679)		8-14EM (N=1084)		4-7EM (N=959)	
	n	%	n	%	n	%
Pain/Body	638	94%	1017	94%	863	90%
Mood and cognition	622	92%	994	92%	829	86%
Environmental handicap	600	88%	949	88%	793	83%
Depression symptoms	411	61%	539	50%	393	41%
Sleep alterations	282	42%	393	36%	221	23%
Others	250	37%	258	24%	188	20%
No symptoms	112	16%	224	21%	135	14%

Abbreviations: EM, episodic migraine; CM, chronic migraine

Table 1. Symptoms related to absenteeism due to migraine reported by employed migraineurs (N=2722)

Conclusion: Migraine is reported to have a considerable impact in the lives of affected individuals with symptoms impacting the work productivity of employed migraineurs.

Disclosure: This study was sponsored by Novartis Pharma AG, Basel, Switzerland

Movement disorders 5

EP3082

An observational study of rotigotine transdermal patch and other currently prescribed therapies in patients with Parkinson's disease

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Background and aims: To describe real-world management of Parkinson's disease (PD) with dopaminergic treatments and the influence of routinely used management strategies on clinical outcomes. The study was also part of a European Medicines Agency risk-management plan for the non-ergoline dopamine agonist (DA) rotigotine, focusing on cardiovascular fibrosis.

Methods: SP0854 (NCT00599339) was a prospective, multicentre (10 countries), non-interventional post-authorisation safety study of rotigotine and other dopaminergics, conducted under standard medical practice. Patients requiring either monotherapy (rotigotine/other DAs/levodopa), or levodopa in combination with rotigotine/other DA, were included and followed for ≤33 months. Baseline intended patient-ratio: 5:2:2:5:2 for "rotigotine", "other DA", "levodopa", "levodopa+rotigotine", "levodopa+other DA". Treatment modifications were allowed according to patients' needs. Primary safety objective: evaluation of cardiovascular fibrosis. Primary efficacy variable: change from baseline in UPDRS-III (motor), assessed by treatment received at a particular post-baseline visit.

Results: 1531/2195 (69.7%) patients completed the study. Discontinuation reasons: lost to follow-up (221;10.1%), consent withdrawn (137;6.2%), adverse events ([AEs] 79;3.6%), other (179;8.2%). Demographics/disease characteristics: Table 1. 5 (0.2%) patients experienced AEs of structural cardiovascular pathology: Table 2. Overall AEs: Table 2. Mean UPDRS-III score numerically improved when assessed by treatment received at Month 15, and in most treatments received at Month 33 (Figure 1).

Table 1. Baseline demographics and disease characteristics (safety set)

	All patients N=2179
Age, mean ± SD, years	67.7 ± 9.4 (n=2146)
Gender, n (%)	
Male	1199 (55.0)
Female	946 (43.4)
Race, n (%)	
White	2078 (95.4)
Black	2 (0.1)
Asian	2 (0.1)
Other	63 (2.9)
Years since PD diagnosis, mean ± SD	2.59 ± 3.61 (n=2034)
Hoehn & Yahr stage, during 'on', n (%) ^a	
0	8 (0.4)
1	501 (23.0)
2	1014 (46.5)
3	515 (23.6)
4	96 (4.4)
5	8 (0.4)
Dopaminergic PD therapy at study onset, n (%)	
Dopaminergic monotherapy (rotigotine, other DA, or levodopa)	1462 (66.8)
Levodopa in combination with rotigotine or other DA	603 (27.5)
Other dopaminergic PD therapy ^b	63 (2.9)

^aData from patients without valid data consent form (n=54 in safety set) were not used for analysis. The denominator for all %s presented in the full safety set (i.e. 2179), therefore total %s do not add up to 100.
^bHoehn & Yahr stage data missing for 3 patients.
^cOther dopaminergic PD therapy, defined as therapy with multiple DAs without levodopa, or not treated with dopaminergic therapy (i.e. delay in start of PD treatment).

Table 1

Table 2. Overview of adverse events (safety set)

MedDRA Preferred term	All patients n (%) [AEs]
Overview of AEs of structural cardiovascular pathology (AE of special interest)	
All	5 (0.2) [6]
Cardiac valve disease	2 (0.1) [2]
Cardiac valve sclerosis	2 (0.1) [2]
Aortic valve sclerosis	1 (0.1) [1]
Serious AE	2 (0.1) [2]
Intensity of AE	
Mild	4 (0.2) [4]
Moderate	1 (0.1) [1]
Final outcome of AE	
Recovered	2
Not recovered, ongoing	1
Lost to follow-up	2
Temporarily associated with rotigotine ^a (n=1392)	1 (0.1) [2]
Not temporarily associated with rotigotine ^a (n=1328)	3 (0.3) [3]
Causally related to rotigotine ^b	0
Causally related to other dopaminergic study medication ^c	2
Overview of all AEs	
All AEs	1501 (68.9) [1613]
Serious AE	504 (23.1) [509]
AE leading to discontinuation of at least one PD medication	188 (8.6) [232]
AEs with an incidence of at least 0%	
Fluores	183 (8.4) [233]
Parkinson's disease	164 (7.5) [202]
Application and initiation type reactions ^d	145 (6.7) [161]
Fatigue	141 (6.5) [156]
Depression	134 (6.1) [137]
Fall	129 (5.9) [156]
Back pain	125 (5.7) [147]

AE, adverse event; n = number of patients reporting at least 1 AE; % = percentage of patients among the total N (AEs) / total number of patients.
^aTemporarily associated with rotigotine: 1 = count of individual AEs occurring among the 1392 patients, who was considered to be temporarily associated with rotigotine if rotigotine was administered at least once within 30 days prior to the onset of the AE.
^bTemporarily associated with rotigotine: 1 = study physician considered a causal relationship of the AE to treatment with rotigotine.
^cThe study physician considered a causal relationship of the AE to treatment with study medication (other than rotigotine): 1 = with cabergoline and 1 with bromocriptine.
^dMedDRA high level term.

Table 2

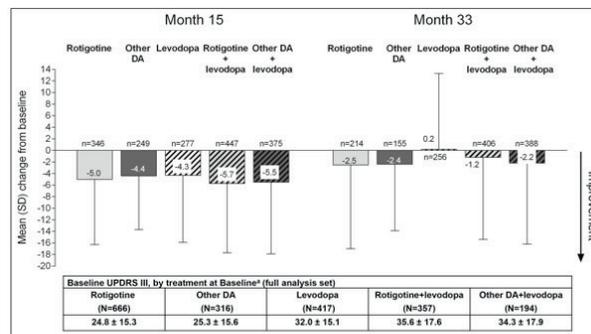


Figure 1. Change from baseline in UPDRS III by treatment at visit: Month 15 and Month 33 (full analysis set). Changes from baseline data are reported by the treatment a patient was receiving at the particular visit (at Month 15 and at Month 33); patients were not necessarily receiving that treatment at baseline. UPDRS, Unified Parkinson's Disease Rating Scale.
^aOnly those treatments reported by ≥100 patients at baseline are reported; at baseline, 19 patients were receiving multiple DAs, 24 receiving multiple DAs+levodopa, and 33 were not treated (delay in start of treatment).

Figure 1

Conclusion: This study reports real-world data from >2000 PD patients receiving dopaminergic treatment for up to 3 years. Few patients (5) experienced AEs of structural cardiovascular pathology; none were considered causally-related to rotigotine, and no new safety signal was observed. UPDRS results suggest adequate control of motor symptoms with dopaminergic treatment over time.

Funding: UCB Pharma.

Disclosure: Thomas Müller, Eduardo Tolosa, Letitia Badea and Lars Timmermann were study investigators on this UCB Pharma-funded study; Frank Grieger, Michael

Markowitz, Xavier Nondonfaz, and Lars Bauer are salaried employees of UCB Pharma, and receive stock options from their employment; Mahnaz Asgharnejad is a former salaried employee of UCB Pharma, and received stock options from her employment.

EP3083

Cardiac autonomic testing in Parkinson's disease and multiple system atrophy: A possible discriminating tool?

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Background and aims: The differential diagnosis of Parkinson's disease (PD) and multiple system atrophy (MSA) is difficult yet crucial. The aim of this study was to compare the neurophysiologic cardiac autonomic findings in these two degenerative diseases.

Methods: Retrospective study (from January 2015 to December 2016) including patients diagnosed with PD or MSA who had clinical cardiac autonomic function tests carried out according to Ewing's battery. We assessed cardiac parasympathetic (Heart rate variation to deep breathing(HR-DB), to Valsalva(HR-V), heart rate response to standing(HR-S)) and sympathetic (sympathetic skin response(SSR)) autonomic system. Patients were graded as per Ewing's criteria into normal, early or definite autonomic dysfunction.

Results: We collected 65 patients: 42PD and 23MSA (respectively: sex-ratio=2.8 and 0.8; dysautonomic complaints in 90.4%PD and 95.6%MSA). Neurophysiologic dysautonomia was found respectively in 95.2% of PD and 100% of MSA. HR-DB was altered respectively in PD and MSA in 4.7% and 8.7% (mean variation=37 and 32.6), HR-V in 38% and 39% (mean variation=1.53 and 1.56) and HR-S in 78.5% and 82.6% (mean response=1.07 and 0.96). Parasympathetic dysautonomia was, respectively in PD and MSA, early in 66.6% and 47.8%, and definite in 26.2% and 43.5%. Sympathetic dysautonomia was associated in 16.6% in PD and 47.8% in MSA (p=0,009) and isolated in 2.4% of PD and 13% of MSA.

Conclusion: Our study showed that neurophysiologic autonomic dysfunction was constant in MSA. The association of sympathetic and parasympathetic dysautonomia was significantly more suggestive of MSA rather than PD. Further studies on larger cohorts are required to confirm these findings.

Disclosure: Nothing to disclose

EP3084

Cancelled

EP3085

Cancelled

EP3086

'Advanced' Parkinson's disease characteristics in clinical practice: Results from the OBSERVE-PD study, a cross-sectional observational study of 2615 patients

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Background and aims: 'Advanced' Parkinson's disease (PD) patients are often treated at specialized movement disorder centres. However, the defining features of 'advanced' PD patients are not well understood. This study characterized the clinical and non-clinical features and treatments (including device-aided options) in PD patients considered 'advanced' by movement disorder specialists.

Methods: A cross-sectional, observational study was conducted at 128 movement disorder centres in 18 countries. The primary outcome was the proportion of PD patients identified by their physician as 'advanced'. The clinical and non-clinical characteristics of 'advanced' and 'non-advanced' patients were compared using descriptive statistics. Physicians' assessment of 'advanced' PD was compared to a Delphi-criteria-based classification.

Results: According to the physicians' judgment, 51.3% (n=1342/2615) of PD patients were considered 'advanced', but this proportion varied regionally. A moderate correlation existed between the physician's judgment and the Delphi-consensus-based criteria for 'advanced' PD. 'Advanced' and 'non-advanced' patients were similar regarding age, gender, and living situation, but differed in terms of motor symptom severity (Unified Parkinson's Disease Rating Scale [UPDRS] Part III score), motor fluctuations (UPDRS Part IV Q32 and Q39), non-motor symptoms (NMS) (NMS Scale total score), quality of life (8-item Parkinson's Disease Questionnaire total score) and caregiver support status (Table). Of the 'advanced' patients 882/1342 (66%),

were eligible for device-aided treatment, and 548 (41%) had ongoing device-aided treatment or were about to start.

Table: Characteristics of Advanced and Non-advanced Parkinson Disease Patients

Characteristics	Advanced PD, N=1342		Non-advanced PD, N=1273	
	n/N (%)	Mean [SD]	n/N (%)	Mean [SD]
Age, years		67.6 [9.4]		66.4 [10.3]
Sex, male	817/1342 (61)		734/1273 (58)	
Living at home	1304/1342 (97)		1264/1273 (99)	
Caregiver support, yes	917/1327 (69)		328/1270 (26)	
Time since diagnosis, years		11.0 [5.8]		4.3 [3.7]
Motor fluctuations present, yes	1167/1342 (87)		295/1273 (23)	
Duration of motor fluctuations, years ^a		4.9 [3.9]		2.3 [2.1]
UPDRS II (ADL), score ^b		16.5 [8.3] ***		8.4 [5.4] ***
UPDRS III (motor), score ^c		30.2 [14.7] ***		21.1 [11.0] ***
UPDRS IV Q32, dyskinesia, none	501/1338 (37)		1097/1268 (87)	
UPDRS IV Q39, off time, none	271/1336 (20)		931/1259 (74)	
UPDRS V: Modified Hoehn & Yahr, score ^d		2.9 [0.8] ***		2.0 [0.6] ***
NMSS, total score ^e		58.6 [43.0] ***		34.4 [30.9] ***
PDQ-8, total score ^f		36.6 [19.3] ***		20.7 [16.4] ***
Eligible for invasive treatment options, yes	882/1342 (66)		127/1272 (10)	
Status of invasive treatment for eligible patients				
Ongoing	384/882 (44)		15/127 (12)	
Decided at visit to start	164/882 (19)		17/127 (13)	
No	332/882 (38)		91/127 (72)	
Missing	2/882 (0.2)		4/127 (3.1)	

N for advanced PD, non-advanced PD: a. 1151, 272; b. 1341, 1270; c. 1341, 1272; d. 1342, 1272; e. 1070, 1018; f. 1326, 1262. The UPDRS was measured in the 'on' state. Statistical significance based on a t-test between the Advanced and non-advanced PD patients are indicated at the P<0.0001 (***). All proportions except for the invasive treatment status included patients with non-missing data. UPDRS = Unified Parkinson's Disease Rating Scale; NMSS = Non-motor Symptom Scale; PDQ-8 = 8-item Parkinson's Disease Questionnaire

Conclusion: This study demonstrated that physicians judged more than half of the PD patients in movement disorder centres across 18 countries as 'advanced', with distinct characteristics regarding motor fluctuations, non-motor symptoms and quality of life.

Disclosure: AbbVie funded the work and participated in the study design, research, data collection, analysis and interpretation of data, reviewing, and approving the publication; medical writing support was provided by Jane M. Rodgers and Amy M. Spiegel, of AbbVie Inc.

EP3087

A study assessing the effect of a structured medication review on quality of life in patients with Parkinson's disease: An interim analysis

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Background and aims: To investigate whether a structured medication review (SMR) executed by community pharmacists leads to better quality of life (QoL) in patients with Parkinson's disease (PD). The secondary objectives are measurements of activities of daily life, presence of non-motor symptoms, disease perception and quality of life of personal caregivers.

Background: Treatment of PD is symptomatic and frequently consists of complicated medication. This negatively influences therapy adherence, resulting in a substantial lower benefit of treatment and a decreased QoL. Little is known about the effects of a SMR on QoL and the feasibility of medication assessment within primary care.

Methods: In this multicenter randomized controlled study, 108 PD-patients with ≥ four different medications and ≥ four different medication intake moments daily were included. The intervention consisted of a SMR performed by community pharmacists. Primary outcome was PD-specific QoL (PDQ-39). Measurements were performed at baseline, 3 and 6 months of follow up. Analyses were performed using linear mixed model repeated measurements analyses.

Results: A total of 108 of the 200 patients were thus far included with a mean age of 74.2 years (SD±7.0), 8.2 (SD±2.8) different medications and 5.2 (SD±1.8) medication intake moments daily. After six months, there was no significant difference in overall score of the PDQ-39, although a clinically and statistically significant difference was found in the domain 'emotional well-being', in favour of the control group (Table 1).

PDQ-39	Intervention group (SMR)			Control group (usual care)			Treatment effect at 6 months Δ I-CI (95% CI)	P-value [†]
	Baseline (n=44)	3 mo. (n=30)	6 mo. (n=31)	Baseline (n=64)	3 mo. (n=47)	6 mo. (n=41)		
Overall score	35.6 (2.4)	38.6 (2.8)	38.3 (2.9)	36.3 (2.0)	37.0 (2.3)	37.9 (2.4)	-1.2 (-5.5; 3.2)	0.69
Mobility	44.0 (3.9)	45.6 (4.2)	45.2 (4.3)	46.4 (3.2)	46.4 (3.4)	45.9 (3.6)	-1.7 (-8.3; 4.9)	0.85
Activities of daily living	42.5 (3.8)	44.8 (4.3)	46.9 (4.2)	41.9 (3.2)	43.5 (3.5)	44.7 (3.5)	-1.5 (-7.2; 4.1)	0.86
Emotional well-being	27.8 (2.8)	37.4 (4.9)	35.0 (3.3)	31.8 (2.4)	32.8 (4.0)	32.4 (2.8)	-6.6 (-12.7; -0.5)*	0.07
Stigma	19.5 (2.8)	21.7 (3.5)	21.1 (3.5)	21.6 (2.3)	23.2 (2.8)	22.7 (3.0)	-0.5 (-8.6; 7.5)	0.99
Social support	23.5 (3.9)	28.1 (4.2)	26.8 (4.4)	24.5 (3.2)	27.6 (3.4)	27.5 (3.7)	-0.2 (-8.9; 8.5)	0.94
Cognition	35.1 (2.9)	39.4 (3.1)	39.7 (3.3)	33.6 (2.4)	38.4 (2.5)	37.7 (2.8)	-0.5 (-8.4; 7.5)	0.86
Communication	33.0 (3.1)	32.8 (3.4)	32.8 (3.8)	27.0 (2.6)	25.0 (2.8)	29.7 (3.2)	2.8 (-8.3; 12.0)	0.55
Pain	46.6 (3.0)	46.2 (3.8)	48.1 (3.4)	45.0 (2.5)	43.3 (3.1)	47.1 (2.9)	0.6 (-7.0; 8.1)	0.86

Table 1 Outcomes of the PDQ-39 questionnaire data (range 0 (best QoL) - 100 (worst QoL), analysed by 'Repeated measurement analysis', presented as mean (SE). * Exceeds the minimally important difference determined by Peto et al. †SMR: Structured medication review. ‡I-C: Intervention group minus Control group; a positive change is in favour of the intervention group. †P-value based on 'group-by-time interaction'.

Conclusion: In this interim analysis, QoL in PD-patients did not improve six months after performing a SMR executed by community pharmacists.

Disclosure: Nothing to disclose

EP3088

A pilot study to examine the single dose pharmacokinetic properties of two formulations of Apomorphine Sublingual Film (APL-130277) 15 mg in health volunteers

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Background and aims: APL-130277 (apomorphine) is administered sublingually and being studied for OFF episodes. The primary objective of this study was to evaluate the pharmacokinetics (PK) parameters of a single 15 mg dose of APL-130277 in healthy volunteers and compare the bioavailability between the formulation used in study CTH-105 and the scaled-up formulation.

Methods: Twelve healthy male volunteers between 21 and 60 years inclusive were enrolled. All subjects received APL-130277 (CTH-105 formulation [drug-side facing up towards the tongue]), APL-130277 (scaled-up formulation [buffer-side facing up towards the tongue]), and APL-130277 (scaled-up formulation [drug-side facing up towards the tongue]) dosed on three separate days, crossed over with a 24-hour washout. PK assessments were evaluated from 0 to 12 hours post dosing. Subjects were pretreated with domperidone BID starting on Day -3. Study subjects and clinical staff members (except the staff member responsible for dosing) were blinded.

Results: The PK parameters were similar between the two formulations [i.e., CTH-105 formulation and the scaled-up formulation, irrespective of the orientation of the film under the tongue] (Table 1). The plasma apomorphine concentration was similar at all timepoints with the scaled-up formulation, irrespective of the orientation of the film under the tongue (Figure 1).

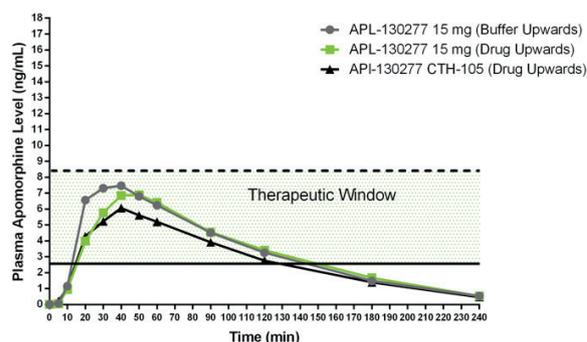


Figure 1: Plasma Apomorphine Level (ng/mL) Over Time: Scaled Up Formulation

Conclusion: These results indicated that the two formulations display very similar pharmacokinetic profiles with respect to C_{max} and AUC values. The orientation of the film under the tongue for the scaled-up formulation did not have a meaningful impact on the bioavailability of the drug.

Disclosure: The study was funded by Sunovion CNS Development Canada ULC. Eric J. Pappert is employed by Sunovion Pharmaceuticals, Inc. Peter Gardzinski, Thierry Bilbault, and Albert Agro are employed by Sunovion CNS Development Canada ULC.

Table 1: Descriptive Statistics of the Pharmacokinetic Parameters for Plasma Apomorphine

Treatment 15 mg APL-130277	$t_{1/2}$ (hr) mean	C_{max} (ng/mL) mean	AUC _{last} (min*ng/mL) mean	AUC _{inf} (min*ng/mL) mean	MRT (min) mean
CTH-105 Formulation (drug side facing up towards to tongue)	50.6	6.41	650	685	100
Scaled-Up Formulation (buffer side facing up towards to tongue)	52.6	8.45	781	823	99.6
Scaled-Up Formulation (drug side facing up towards the tongue)	46.9	7.30	760	797	100

AUC=area under the plasma concentration vs. time curve (min*ng/mL); C_{max} =maximum plasma concentration; MRT=mean residence time; $T_{1/2}$ =time from dosing to C_{max}

Table 1: Descriptive Statistics of the Pharmacokinetic Parameters for Plasma Apomorphine

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EP3093

Influence of food on Opicapone pharmacokinetics and pharmacodynamics

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Background and aims: To characterize the effect of food on the pharmacokinetics (PK) and pharmacodynamics (PD) of opicapone (OPC) after single and repeated doses.

Methods: Two open-label studies were conducted: Study-1 was a 50mg OPC single-dose, 2-period, 2-sequence, crossover fast versus fed (high-fat and high-caloric meal) study in 12 healthy subjects; Study-2 was a 12-day fasting once-daily 50mg OPC single-arm study in 28 healthy subjects, for which on day 10 OPC was administered in the evening with a moderate meal.

Results: In Study-1, following a 50mg OPC single-dose, the OPC rate and extent of absorption were significantly lower in the fed state compared to the fasted state (fed:fasted ratios of 31.73% for C_{max} and 47.11% for AUC_t). The t_{max} was also significantly increased by the presence of food. In Study-2, following once-daily 50mg OPC, the OPC rate and extent of absorption were significantly lower in the fed state (day 10) compared to the fasted state (day 9, fed:fasted ratios of 38.21% for C_{max} and 68.70% for AUC_t). The t_{max} was also significantly increased by the presence of food. However, despite AUEC being slightly higher (with upper limit of the 90%CI just outside the pre-specified acceptance interval of 80-125%), following a moderate meal (day 10), E_{max} and the threshold of efficacy, i.e., every 24 hour effect (E_{min}) of COMT were not affected in a relevant way.

Conclusion: Opicapone was safe and well tolerated and at steady-state, can be administered concomitantly with a moderate meal without affecting its COMT inhibition.

Disclosure: Nothing to disclose

EP3094

Opicapone's bedtime regimen and the decision-making process

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Background and aims: To clarify the decision-making process for opicapone's bedtime regimen.

Methods: Review of opicapone, levodopa, carbidopa and benserazide pharmacokinetic data. Five phase-1 studies were selected on the basis of concomitant, alone or 1-hour apart administration between oral single-doses of opicapone (25, 50 and 100mg) and immediate- (IR) or controlled-release (CR) levodopa/carbidopa (LC, 100/25) or levodopa/benserazide (LB, 100/25).

Results: In studies conducted with IR/CR-LB concomitant administration, an increase in rate (C_{max}) and extent (AUC) to levodopa and benserazide occurred at all doses of opicapone. The increase was statistically significant for IR formulation. Levodopa C_{max} decreased when doses of opicapone increased. In studies conducted with IR/CR-LC concomitant administration, a statistically significant increase in C_{max} and AUC to levodopa, but not to carbidopa, occurred at all doses of opicapone. Levodopa C_{max} decreased (more pronounced with CR formulation) when doses of opicapone increased. Similar levodopa and carbidopa C_{max} was observed when opicapone (50mg) was administered 1-hour apart from IR-LC. Opicapone's systemic exposure increased in a dose-proportional manner but an important variability was observed between different levodopa formulations and the use of carbidopa/benserazide.

Conclusion: The pharmacokinetic data suggest a certain degree of interaction at absorption phase that was minimized by separating both administrations for at least 1-hour. Opicapone was developed as an add-on to levodopa and, taking into consideration that Parkinson's disease patients may well necessitate several daily doses of levodopa, a bedtime regimen for opicapone was proposed to better allow the physician to individually tailor the levodopa daily regimen without any concern of a potential absorption interaction.

Disclosure: Nothing to disclose

EP3095

Visual hallucinations related to Parkinson's disease in Polish patients.K. Smilowska¹, M. Smilowski², L. Szczechowski³¹Katowice, Poland, ²Neurology, Multiklinika Salute, Katowice, Poland, ³Neurology, Multiklinika Salute, Katowice, Poland

Background and aims: Visual hallucinations (VH) are one of neuropsychiatric non-motor symptoms of Parkinson's Disease (PD). VH are mostly drug-induced but neurodegeneration, as primary reason, should also be considered. The aim of the study was to evaluate prevalence and clinical correlations of PD patients in Polish population.

Methods: 110 patients diagnosed with idiopathic PD according to UK Parkinson's Disease Society Brain Bank Criteria were enrolled into the study. All patients underwent Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) and Non-Motor Symptoms Questionnaire (NMS-Quest) evaluation and depression screening based on Hamilton Depression Rating Scale (HAM-D).

Results: Visual hallucinations occurred in 20.99% (n=23). The positive correlation was observed between hallucinations and patient's age as well as disease duration. Disease severity assessed in UPDRS part III was greater among patients with VS. Depression rate was higher in non-hallucination PD patients group.

Conclusion: Visual hallucinations are frequent among PD patients. Older patients with longer disease duration and greater disease severity are in a risk group of VH occurrence. Variability of VH is fascinating – from simple to complex and sophisticated.

Disclosure: Nothing to disclose

EP3096

Brain atrophy in Wilson's disease is related to neurological impairment and copper metabolismL. Smolinski¹, T. Litwin¹, B. Redzia-Ogrodnik²,K. Dziezyc¹, A. Czlonkowska¹¹2nd Department of Neurology, Institute of Psychiatry and Neurology, Warsaw, Poland, ²Department of Radiology, Institute of Psychiatry and Neurology, Warsaw, Poland

Background and aims: Brain atrophy is a prominent neuroimaging feature of Wilson's disease (WD). However, it is usually assessed qualitatively, and the relationship between quantitative measures of brain atrophy, neurological impairment, and copper metabolism in WD has not been investigated. Therefore, we aimed to address this issue.

Methods: We retrospectively analysed 47 newly diagnosed WD patients in whom brain MRI and copper metabolism studies were performed before treatment initiation. Neurological deficits were assessed on the Unified Wilson's Disease Rating Scale (UWDRS). Brain parenchymal fraction (BPF, i.e. brain volume normalized for intracranial volume) was calculated for each participant with Statistical Parametric Mapping software (v.12). Copper metabolism consisted of serum concentrations of ceruloplasmin, total copper, and non-ceruloplasmin bound copper (NCC). Statistical analysis included correlations between UWDRS, copper metabolism, and BPF.

Results: UWDRS scores correlated significantly with BPF ($r=-0.631$, $p<0.001$), and both UWDRS and BPF correlated with age at diagnosis ($r=0.392$, $p=0.006$ for UWDRS; $r=-0.690$, $p<0.001$ for BPF). The relationship between BPF and UWDRS remained significant after controlling for age and gender ($r=-0.535$; $p<0.001$). Moreover, after accounting for gender and age at diagnosis, both UWDRS and BPF correlated with the serum NCC concentration ($r=0.285$; $p=0.037$ for UWDRS; $r=-0.295$; $p=0.032$ for BPF). Ceruloplasmin and total serum copper were not significantly related to UWDRS scores nor to BPF.

Conclusion: Brain atrophy is related to neurological impairment in patients with WD and is associated with serum NCC concentration.

Disclosure: Nothing to disclose

EP3097

Differentiation between Lewy body diseases and atypical parkinsonian syndromes using combined brain SPECTs

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Background and aims: Neuroimaging facilitates the differential diagnosis of movement disorders. We aimed to assess whether an automated analysis of combined dopamine transporter (DA) and perfusion single photon emission computed tomography (SPECT) could discriminate patients with Lewy body diseases (LBD), including idiopathic Parkinson disease (PD) and diffuse Lewy body disease (DLB), and atypical parkinsonian syndromes (APS), including multiple system atrophy (MSA), progressive supranuclear palsy (PSP) and corticobasal syndrome (CBS).

Methods: We examined consecutive 32 patients with LBD and 21 patients with APS. The clinical diagnosis of each disease was made based on published criteria without imaging data. Anatomical MRI was segmented into cortical and subcortical regions using an automated process. Then, 123I-ioflupane (123I-FP-CIT)- and 123I-iodoamphetamine (IMP)-SPECT data were coregistered onto the anatomical MRI in each patient using mutual information algorithm. DAT activity and regional perfusion in each brain region were extracted in each patient and submitted to a logistic regression analysis as independent variables. A stepwise procedure was used to select predictive variables that should be included in the model to differentiate LBD and APS. Receiver operating characteristic (ROC) analysis was performed to measure diagnostic power.

Results: The stepwise logistic regression analysis yielded three predictive variables; striatal DAT activity, the regional perfusion in the lenticular nucleus and midline frontal lobe. ROC analysis revealed that the area under the curve was 0.876 (sensitivity 84.4%, specificity 90.5%).

Conclusion: An automated classification using combined dopamine transporter and perfusion SPECTs showed a high accuracy in distinguishing patients with LBD and APS without clinical information.

Disclosure: This study was supported by Nihon Medi-Physics Co., Ltd. The sponsor had no role in the study design, data collection, data analysis, data interpretation, or writing of this report.

EP3098

Parkinsonism in Kennedy's disease (spinal and bulbar muscular atrophy, SBMA)

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Background and aims: Kennedy's disease (SBMA) is a rare, adult-onset, X-linked, recessive trinucleotide, neuromuscular disease, caused by expansion of a CAG-tandem-repeat in exon 1 of the androgen-receptor (AR) gene on chromosome Xq11-12.

Methods: Case report.

Results: We present the case of a 72-year-old male patient who developed the symptoms of parkinsonism in 2011 - bilateral rigidity, bradykinesia, frequent falls with early postural instability - and five years later he developed the symptoms of Kennedy's disease. In 2014 progressive dysphagia has been formed and from 2016 bulbar and spinal symptoms have appeared (perioral and lingual tremor, fibrillation, weakness and wasting of facial, bulbar, glossal and upper limb muscles, fasciculation, dysarthria, dysphagia, reduced deep tendon reflexes). At the last clinical admission beside the symptoms mentioned above we observed gynecomastia in July 2016. The fast progression of the parkinsonism has to be mentioned. Considering the clinical data and electrophysiological results we thought of the possibility of Kennedy's disease. The genetic testing gave the final diagnosis: SBMA (CAG-tandem-repeat number in exon 1 of the AR gene on chromosome Xq12: 44+/-1).

Conclusion: This is one of the first reported cases of Kennedy's disease with parkinsonism. Another lesson of the case is severe progressive dysphagia may be the manifestation of a rare genetic disorder.

Disclosure: Nothing to disclose

EP3099

Cancelled

EP3100

The INVEST study: A comparison of deep brain stimulation and continuous intrajejunal levodopa infusion in advanced Parkinson's disease

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Background and aims: Deep brain stimulation (DBS) and continuous intrajejunal levodopa infusion (CLI) are both efficacious treatments of motor symptoms in advanced Parkinson's disease (PD). They reduce medication induced motor fluctuations and dyskinesias. Moreover, they significantly improve quality of life. The costs of CLI seem higher. Yet, comparative knowledge with respect to effectiveness, complications and costs is lacking as a randomized controlled trial (RCT) comparing DBS and CLI has never been performed. As a result, there is unwanted variation in medical practice regarding treatment of advanced PD.

Methods: A prospective open label multicentre RCT is currently performed. A total of 66 PD patients with medication induced motor fluctuations will be randomised between DBS and CLI treatment. Patients not willing to be randomised are eligible for an observational patient-preference study. There are 6 assessment visits in the first year of treatment. The primary health economic outcomes are costs per unit on the quality of life scale PDQ-39 and costs per QALY (Quality Adjusted Life Years) at 12 months. Major secondary outcomes are quality of life, functional health and complications.

Results: The study started in December 2014, results are expected in 2019.

Conclusion: The INVEST study is the first randomised study to provide comparative knowledge on the therapies DBS and CLI in advanced PD.

Disclosure: Dr. Dijk, Dr. de Bie and Mr. van Poppelen are researchers of the INVEST study. This investigator initiated multicentre trial is funded by ZonMw Doelmatigheid, project number 837002509 and by an unconditional grant of Medtronic Netherlands.

EP3101

Gray matter atrophy in Parkinson's disease and freezing of gait reflected by software package Freesurfer

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Background and aims: Freezing of gait (FOG) is a troublesome symptom of Parkinson's disease (PD). The relationship between regional brain atrophy and FOG has been poorly investigated. Using Freesurfer software we tested whether gray matter (GM) atrophy contributes to FOG in PD.

Methods: We investigated 20 patients with PD, 10 with FOG and 10 without FOG, both groups of patients were assessed using FOG questionnaire, "Time up and go" test, Hoehn and Yahr staging. High resolution T1-weighted brain images were acquired for each subject using a 1.5T MRI scanner. A surface-based method implemented in FreeSurfer was used to quantify GM atrophy. A vertex-wise and region of interest (ROI) two-sample t-test of normalized subject data was used to assess significant group differences. The analysis was controlled for age, gender and total intracranial volume.

Results: Gray matter was significantly reduced in the pre-supplementary motor area in freezers, compared to matched nonfreezers at $p < 0.001$, uncorrected. The ROI (region of interest) analysis controlled for age, gender and intracranial-volume yielded further differences in gyrus cinguli (in the anterior part), in supplementary motor area (SMA) on the left side, in the area of frontal operculum on the right side. FOG- groups of our patients reported greater atrophy in the occipital cortex. Higher global level of cortical atrophy were detected in freezers.

Conclusion: Our findings provide the additional evidence that the development of FOG in patients with PD is associated with local GM atrophy, which may play a role in the complex pathophysiology of this disabling symptom.

Disclosure: Nothing to disclose

EP3102

A clinical and genetic study of Huntington's disease, based on our Bulgarian team's 9 year experience

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Background and aims: Huntington's disease (HD) is a rare neurodegenerative disorder characterized by chorea, psychiatric disturbances and dementia. We aim to review the demographics, clinical and genetic features of HD in Bulgaria and create a local patient database.

Methods: The patients underwent clinical, neurophysiological examinations, brain magnetic resonance/ computed tomography imaging and molecular genetic studies.

Results: A total of 80 symptomatic individuals from 60 families, belonging to two large ethnic groups (Bulgarian and Turkish) were evaluated. There were no families from the Roma ethnic group. The affected originated from different regions in Bulgaria. HD was confirmed through genetic tests on 64 individuals, of whom 63 were symptomatic and 1 asymptomatic. The gene was inherited maternally in 28 and paternally in 18. In 4 participants there was no known family history, and in 14 the information was missing. Motor onset was the most common, followed by mixed onset (motor and cognitive signs) and non-motor onset (psychiatric problems). The age at onset varied from 17 to 66 years. Most participants were undergoing treatment for hyperkinesia with Haloperidol. According to family history, 60 additional family members showed signs of HD.

Conclusion: The observed phenotypes and genotypes are similar to those reported in literature. Anticipation and genome imprinting were also detected. Creation of a local patient database will help us with regular monitoring and timely implementation of latest therapeutic strategies.

Disclosure: Nothing to disclose

EP3103

Cancelled

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EP3104

Comparison of fingolimod and teriflunomide on the basis of early relapse risk following the switch from injectables in patients with stable multiple sclerosis

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Background and aims: Both fingolimod and teriflunomide are oral agent effectively used in multiple sclerosis (MS). The aim of this study was to determine early relapse possibilities in multiple sclerosis (MS) patients switching to oral therapy following a period of stable disease on IFN β or GA and to compare fingolimod and teriflunomide in this respect.

Methods: A total of 164 patients included in the study from our cohort. Of the total patients, 126 (82.3%) switched to fingolimod, and 29 (17.7%) to teriflunomide. 110 patients were switched from IFN β and 54 patients from GA. Switchers were compared with 124 patients remaining on platform injectables with satisfactory disease control.

Results: Within the switchers, the most frequent reason was lack of tolerance (73.8%). There was no difference in the proportion of patients having at least one relapse in the first 6 months between switchers and patients remaining on platform injectables. The mean annualized relapse rate was 0.03 for switchers, and 0.04 for stayers ($p=0.098$). There was not any difference in disability progression in terms of number of patients in 6 months. There was also no difference between patients switched to fingolimod or teriflunomide in terms of annualized relapse rate ($p=0.12$) and EDSS progression ($p=0.096$).

Conclusion: In conclusion, our results indicated that there was no evidence of disease reactivation within the first 6 months in patients switching to oral therapy when they were previously stable, and both fingolimod and teriflunomide had similar results in this respect.

Disclosure: Nothing to disclose

EP3105

First reported case of Acquired Hemophilia A (AHA) as secondary autoimmune disease following alemtuzumab treatment in multiple sclerosis

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Background and aims: A female patient, 34 y.o. affected by multiple sclerosis since October 2004 experienced a high relapse rate in the first two years and underwent an induction therapy. Therapeutic attempts with mitoxantrone and cyclophosphamide failed in achieving disease stability. From 2008 she underwent 57 cycles of Natalizumab with complete disease control. She decided for three times to discontinue treatment due to PML fear and invariably experienced massive disease reactivation. After the last reactivation we administered two courses of alemtuzumab (January 2015-2016). Since then she had no evidence of clinical or MRI disease activity, and referred high quality of life.

Methods: Clinical case

Results: Since August 2016 she had abnormal bruising for minimal trauma and four haemorrhages: on the left palm after squats, over the dorsalis pedis after tying shoes, over the right hand after having kept her mobile tightly. She was finally admitted at our hospital for limitation in walking abilities due to popliteus muscle's haemorrhage. At blood tests we found high PTT and absence of FVIII. The finding of anti-FVIII antibodies confirmed the diagnosis of AHA. She was treated with rFVII and then with cyclophosphamide 100mg daily for two months and prednisone 100mg daily for a month plus tapering with initial response to treatment. In January 2016, an increase of FVIII-inhibitor without clinical manifestation was found. Due to relapse of AHA we started rituximab 375mg/m² weekly for 4 times.

Conclusion: In MS clinical studies, alemtuzumab-treated patients experienced autoimmune disorders such as AHA (0.2%). PT and PTT should be routinely monitored after alemtuzumab.

Disclosure: Nothing to disclose

EP3106

Mitochondrial targeting therapy: Does it work in MS patients?

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Background and aims: Neurodegeneration has proved to be the major reason of disability in multiple sclerosis (MS). Mitochondrial dysfunction results in functional disturbance without structural damage, then leads to disturbance of respiratory chain function and liberates electrons, giving rise to reactive oxygen species (ROS) and to axonal degeneration, cell death, and tissue destruction. There are no drugs with proven efficacy, nor non-invasive evaluation methods of drug's impact on neurodegeneration in central nervous system.

The aims of our research were: 1. to investigate the ability to influence neurodegeneration in MS of Ethyl-methyl-hydroxypyridine succinate (EMHS) – drug with antioxidant and antihypoxant effect, approved in Russian Federation. 2. to reduce the potential of Diffusion tensor MRI with tractography (DTI) as an objective evaluation method of treatments efficacy.

Methods: 51 RR and SP MS patients without signs of disease activity were treated with EMHS, and fractional anisotropy of corticospinal tracts (FA CST) was assessed before and after treatment course.

Results: Compared with 24 healthy volunteers, the patients had significantly lower FA CST. After the treatment, locomotive ability improved as well as FA CST increased, with lasting clinical effect.

Conclusion: The decrease of FA CST is reversible and measuring FA CST can be used as an objective method in evaluating the efficacy of therapy of neurodegeneration in MS patients. EMHS therapy can be considered as a potentially effective method to prevent progressing neurodegeneration in MS patients. However, further controlled clinical trials are necessary in order to prove this effect.

Disclosure: The work was performed as part of state order scientific research at IHB RAS 0133-2016-0005

EP3107

A retrospective comparison of Rituximab vs Cyclophosphamide in neuromyelitis optica spectrum disorders patients

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Background and aims: Neuromyelitis Optica Spectrum Disorders (NMOSD) is a severe demyelinating disease antibody-mediated with no approved treatment. Rituximab (RTX) has been proposed as a first-line therapy, but few comparative studies have been published so far. We retrospectively evaluated the effect of RTX treatment respect to cyclophosphamide (CFX) which is one of the main alternative therapy used in these patients.

Methods: Overall among the 70 NMOSD patients followed at our centre, 42 patients received at least one cycle of RTX and 25 patients received at least two cycles of CFX.

Results: No differences in disease severity and clinical characteristics between the two cohorts were observed (Table1). The median treatment duration was 33 and 11 months for the RTX and CFX group respectively. Overall the proportion of relapse free patients was significantly higher in the RTX group (57% vs 20% $p < 0.0001$) (Fig1). The reduction of the mean ARR was significantly higher in the group of patients receiving RTX (81 vs 43% $p < 0,05$) (Fig2). In both groups the EDSS was stable or improved in the majority of patients (83% in the group treated with RTX and 72% in the group receiving CFX). Since fourteen patients were treated with RTX after the failure of CFX, subgroup analysis confirming the results were performed.

A. Relapse-free survival in overall cohorts

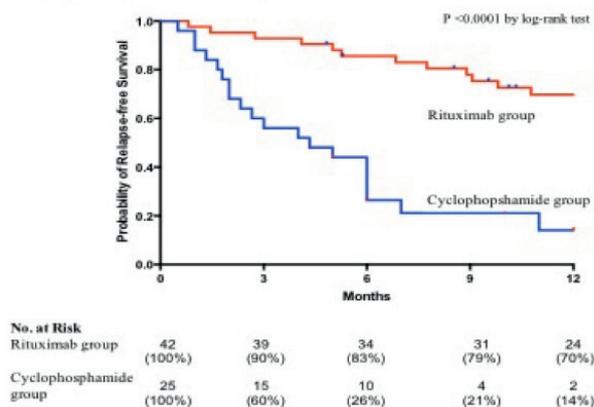


Figure1

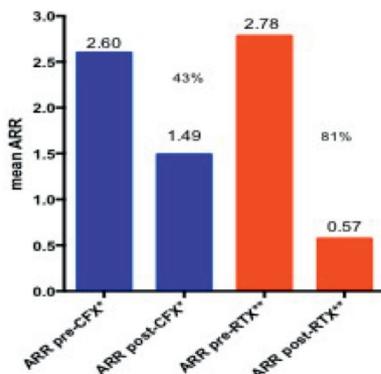
Table 1: comparison of baseline characteristics between CFX population and RTX population.

	Study participants		P value
	Rituximab (n=42)	Cyclophosphamide (n=25)	
2006 diagnostic criteria	22/42 (52%)	12/ 25 (48%)	0.756
Age at disease onset (mean-SD)	39 (15)	39 (15)	0.921
Sex (F)	36/42 (86%)	20/25 (80%)	0.734
AQP4-IgG+	38/42 (90%)	20/25 (80%)	0.277
Disease duration pre RTX/CFX (median-range)	34m (0.5m-28y)	36m (1m-27y)	0.577
EDSS score before RTX/CFX (median-range)	4.00 (2-9)	5.00 (2-8)	0.138
ARR before RTX/CFX (mean-SD)	2.78 (2.7)	2.60 (2.4)	0.622
N° of relapses before RTX/CFX (median-range)	5.0 (1-18)	3.0 (1-17)	0.369
N° of relapses 2 years before RTX (median-range)	3.0 (1-7)	3.0 (1-5)	0.515
N° of therapies before RTX/CFX (mean-range)	1.2 (0-5)	0.6 (0-3)	0.022
Treatment naive patients	14/42 (33%)	16/25 (64%)	0.022

RTX, rituximab; CFX, Cyclophosphamide; AQP4, aquaporin 4; EDSS, Expanded Disability Status Scale; ARR, annualized relapsed rate; m, month; y, year; n°, number

Table1

A. ARR comparison pre- and post- RTX/CFX in whole cohort



* measured on 21/25 patients
** measured on 38/42 patients

Figure2

Conclusion: Our study demonstrated a more efficacy of RTX in NMO patients respect to CFX. Even if our data have to be confirmed in larger study with a longer follow-up, our results justify an earlier use of RTX in clinical practice.

Disclosure: Nothing to disclose

EP3108

Early treatment is associated with a better long-term disability outcome in neuromyelitis optica spectrum disorders

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Background and aims: Neuromyelitis Optica (NMO) is a severe inflammatory disease of the CNS. We report the impact of an earlier treatment in clinical practice.

Methods: We included in our cohort only patients in which, at the end of a thorough investigation, other alternative diagnosis were excluded. Overall 70 patients reached a diagnosis of NMO. We evaluated how treatment approach changes overtime. We divided patients in “early treatment group” if the treatment was started after 1 or 2 relapses and “late-treatment group” if it started after more than 2 relapses.

Results: Overall the number of patients who received an “early treatment” was significantly higher for patients with a disease onset after 2007 (23% vs 50%, p<0.001). In order to test the beneficial effect of an earlier treatment, we excluded 20 patients because they reached a severe disability status within the second relapses. Overall 16 patients were treated “early” and 34 patients were treated “late”. The proportion of patients who reached a severe disability was significantly higher in the “late treatment group” (59% vs 6%; p<0.05). The same results were observed evaluating the proportion of patients developing a permanent EDSS score of at least 6.0 (32% vs 0%; p<0.05) or a permanent severe ipovisus (32% vs 6%; p<0.05).

Conclusion: After the 2006 diagnostic criteria and the definition of NMO SD our treatment approach has significantly changed. An early treatment allowed a better outcome changing the natural history of the disease.

Disclosure: Nothing to disclose

EP3109

Link between overweight/obese in children and youngsters and the occurrence of Multiple Sclerosis

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Background and aims: The prevalence of overweight/obesity is a major problem in the world and the number of MS cases is increasing. This literature study examines the relationship between overweight/obesity in children and adolescents and occurrence of MS.

Methods: We performed a complete literature study resulting in 11 relevant original studies. The search database is primarily Pubmed using MeSH terms "Multiple Sclerosis", "Obesity" and "Overweight" and textwords not to restrict searches.

Results: All 11 relevant included studies show a link between overweight/obesity and the presence of MS among people below 20 years of age. The relation is especially true for young girls. There is a need for more and larger studies, and to investigate the molecular mechanisms that may link obesity and MS.

Conclusion: The literature study convincingly revealed a link between young overweight/obese and occurrence of MS, in particular for girls.

Disclosure: Nothing to disclose

EP3110

Extracellular vesicles in cerebrospinal fluid as possible biomarkers for multiple sclerosis

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Background and aims: Extracellular vesicles (EV) have been suggested as possible carriers of signals related to the pathogenic mechanisms in neurological diseases including multiple sclerosis (MS).

Methods: . We recruited individuals affected by MS at the Neurological Department of our University Hospital. CSF analysis was part of the diagnostic procedure for different neurological diseases. EV were isolated by differential ultracentrifugation of CSF samples, and characterized by flow cytometry. To identify EV origin a panel of fluorescent antibodies was used. CD19, CD200, CD4, CD193 and CD195, IB4. The same IgG labeled isotype of primary antibodies was used as negative control. Statistic analysis were carried out using t test or Mann-Whitney U test to compare subgroups of patients and Kolmogorov Smirnov test was used to compare three or more subgroups of patients.

Results: We analysed CSF by 60 individuals, 38 MS patients, and 22 with neurological disorders. We observed a higher EV concentration in PPMS and in CIS compared to the others. Among relapsing remitting patients EV were more represented during relapses ($p < 0.05$). We detected more IB4 positive EV among PPMS and CIS compared to not inflammatory controls ($p < 0.05$). CD193/CD4+ EV were more expressed in RRMS compared to controls ($p < 0.001$) while we did not detected CD19+ and CD200+ EV.

Conclusion: This study showed a higher EV concentration in MS patients particularly during relapses suggesting that EV concentration may be associated to disease activity. Our study support the hypothesis that EV analyses could represent promising ways to identify new markers underlying molecular mechanisms related to MS pathogenesis.

Disclosure: Dr Sabrina Realmuto received a post doctoral research fellowship, supported by Merck Serono.

EP3111

Impact of a patient support program (REBICARE) on interferon beta 1a adherence and clinical outcomes in relapse-remitting multiple sclerosis

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Background and aims: Poor treatment adherence is a challenge in multiple sclerosis (MS), affecting clinical outcomes and increasing disease burden. This study aimed to assess the impact of a nurse-led support program (REBICARE) on interferon beta 1a adherence among relapse-remitting MS (RRMS) patients in Portugal.

Methods: This was a multicentre, retrospective cohort study consisting of adult RRMS patients who used RebiSmart[®] for ≥ 24 months and started REBICARE between June 2010 and July 2013. The primary endpoint was the proportion of patients who adhered to interferon beta 1a at month 12 (adherence rate $>75\%$). Adherence data was obtained from RebiSmart[®]. Clinical and safety outcomes were assessed through chart review.

Results: Overall, 103 patients were included (mean age 43 years; 69.9% female). Mean duration of MS was 6.6 years and median Expanded Disability Status Score (EDSS) at baseline was 1.75. At Month 12, 99.0% (95% Confidence Interval (CI): 97.1%-100.0%) of patients had an adherence rate $>75\%$. At Month 24, the proportion of patients with adherence $>75\%$ was 98.1% (95% CI: 95.4%-100.0%). The proportion of relapse-free patients at Month 12 and 24 was 81.2% and 72.8%, respectively. The annualised relapse rate was 0.26 at Month 12 and 0.19 at Month 24. Four patients discontinued interferon beta 1a after 24 months. There were no serious adverse events.

Conclusion: This study showed the positive impact of REBICARE on adherence to interferon beta 1a in RRMS patients. This was associated with good clinical outcomes and no unexpected safety issues.

Disclosure: This study was funded by Merck SA.

EP3112

Adherence, cognition and behavioral outcomes in Multiple Sclerosis (MS) patients on dimethyl fumarate – 12-month results of a longitudinal registry study in German MS practices (TREAT)

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Background and aims: (1) to assess adherence, disability, cognition and patient-reported outcomes (PRO) in relapsing-remitting MS (RRMS) patients on dimethyl fumarate (DMF) (first-line treatment or switching from other disease-modifying therapies). (2) to identify relevant factors for non-adherence (discontinuation of study or DMF intake).

Methods: 12-month interim analysis (T12) of a 2-year prospective, multicenter, registry study with assessments at baseline/T0 and at T3, T6, T9, T12, T18 and T24 months. At T12, 721 RRMS patients on DMF (mean age 40.9 yr, 72.4% female, median EDSS 2.0) were analysed. Outcomes: Adherence (yes/no) and time to non-adherence, disability, cognition and PROs representing treatment/life satisfaction, depression, anxiety, fatigue, QoL, disease coping and personality. Descriptive analysis and regression models (logistic and Cox) were used to assess the factors associated with adherence.

Results: All clinical, behavioral and cognitive parameters remained stable during the first 12 months of DMF treatment. By T12, 26.8% (193/721) of patients were non-adherent. Women were more likely to be non-adherent (OR 1.9, HR1.8). The primary reason for non-adherence by T12 was physical complaints (13.0%; 94/721), mainly of gastrointestinal origin (7.9%; 57/721). Univariate (logistic/Cox) regression analyses ($p < 0.15$) identified gender, premedication pause, pre-treatments (≥ 2), depression, QoL, life/treatment satisfaction, fatigue, anxiety and nonverbal memory as putative predictors of non-adherence.

Conclusion: (1) DMF prevents deterioration of clinical, cognitive and behavioral symptoms in RRMS.

(2) Behavioral factors, gender and pre-treatment issues may emerge as predictors of non-adherence.

(3) Multiple regression analyses considering collinearity after 2 years are warranted.

Disclosure: The study was funded by Biogen.

EP3113

MRI in transverse myelitis: Correlation with expanded disability status scale

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*Neurology, Johns Hopkins University, Baltimore, USA***Background and aims:** Magnetic resonance imaging is used as a diagnostic tool to detect spinal cord lesions.

The objective of this paper is to examine cross-sectional correlations of MR images with EDSS. Limited number of studies examined EDSS and MRI correlations in patients with Transverse Myelitis. MRI images can help predict recovery progress based on lesion characteristics.

Methods: We conducted a retrospective review of the last 42 monophasic TM admissions to the Johns Hopkins Hospital. Inclusion criteria included a single inflammatory attack localizing to the spinal cord presenting with a change in neurological examination and a new MRI lesion. Subjects were excluded if their TM was part of a recurring disease or if they tested positive for the NMO-IgG blood test. Extended Disability Status Scale (EDSS) score was calculated at baseline, at presentation, at discharge, and on follow-up. MR images were examined and broken down by Number of Vertebral Bodies Lesion Location Length of the lesion Results of the MRI were compared to the EDSS scores to evaluate outcome based on lesions characteristics.**Results:** Of the 42 subjects enrolled, 37% with Long Lesion (more than 4 vertebral bodies) showed improvement by at least 1 point at one year follow up on EDSS exam. Whereas 19% with Short Lesion (3 or less vertebral bodies) show improvement from admission to one year follow up.**Conclusion:** Longer lesion on MR images from admission to follow up resulted in better long term recovery outcome.**Disclosure:** Nothing to disclose

EP3114

To and from multiple sclerosis: The diagnostic revision dilemmaM. Seabra¹, H. Alves², P. Abreu¹, T. Mendonça³, J. Reis¹, M.J. Sá¹, J. Guimaraes¹¹Porto, Portugal, ²Faculty of Medicine of the University of Porto, Porto, Portugal, ³Neurology, Hospital de São João, Porto, Portugal**Background and aims:** The diagnostic criteria for inflammatory demyelinating diseases (IDDs) of the central nervous system (CNS) evolved over the last years. The close follow-up and accurate multiple sclerosis (MS) diagnosis are key to optimal treatment.**Methods:** The medical records of patients referred to our MS Clinic (n=635), between 2009 and 2016, were retrospectively reviewed to select those who had a diagnostic revision. Sixty-two patients were identified, 44 were misdiagnosed with MS; 18 had another diagnosis, later redefined as MS. Forty-four controls (with MS diagnosis), were matched to the 44 misdiagnosed cases and a statistical analysis was performed to determine predictors of misdiagnosis.**Results:** The mean age of our population (n=44) was 51±11; 77% were women. The mean duration of misdiagnosis was 13 years. Optic neuritis was the most frequent presenting symptom (25%), followed by spinal cord syndrome and nonspecific neurologic symptoms (20% each). The mean EDSS and MSSS was 1.3 (sd=1.9) and 1.8 (sd=2.9) respectively in the misdiagnosed group and 3.7 (sd=2.5) and 3.7 (sd=3) respectively in the control group. From all the variables analysed, the absence of CSF oligoclonal bands (OCB) and MRI findings (dissemination in time) were predictors of misdiagnosis (p<0.05). Conversely, an abnormal autoimmune study and the presenting symptom didn't alter the possibility of a diagnostic error.**Conclusion:** Our series underlines the need to continuously rethink an MS diagnosis and to thoughtfully use paraclinical tests (OCB and MRI) avoiding an unfounded diagnosis. The first event may not be atypical, as reported in other series.**Disclosure:** Nothing to disclose

EP3115

Transcranial sonography and cognitive performance among patients with relapsing remitting multiple sclerosis

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Background and aims: Brain atrophy occurs early in multiple sclerosis. It is associated with cognitive impairment. Transcranial sonography of the brain parenchyma (TCS) can assess ventricular diameter non-invasively, as marker of brain atrophy.

We aimed to correlate cognitive performance among patients with relapsing-remitting multiple sclerosis (RRMS) to ventricular diameters, as a marker of brain atrophy using TCS of brain parenchyma.

Methods: Case-control study, conducted on 125 Egyptian subjects, including 54 multiple sclerosis patients with RRMS, 16 males (29.6%) & 38 females (70.4%), with mean age of 29.22±8.15 SD, mean EDSS of 2.34±1.12 SD & at least 9 years of education. Control group included 71 age, sex and education matched healthy volunteers. All participants were subjected to clinical assessment, cognitive evaluation using California verbal leaning & memory test-2nd edition (CVLT-II), Symbol digit modality test (SDMT) & Controlled oral word association test (COWAT). B-mode TCS of the brain parenchyma was used to evaluate ventricular diameters as parameters of brain atrophy.

Results: In comparison to the healthy control, patients with RRMS showed significantly wider ventricular diameters ($p < 0.001$) denoting brain atrophy. Physical disability & cognitive performance correlated significantly with parameters of brain atrophy. Impairment in executive function is an early marker of CI in patients with RRMS, which was correlated with brain atrophy.

Conclusion: TCS for brain parenchyma is a valuable & easily applicable method in detecting brain atrophy which is correlated with their physical disability & cognitive performance.

Disclosure: Nothing to disclose

EP3116

Clinical features of pseudotumoral Multiple Sclerosis in a Tunisian cohort

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Background and aims: Multiple sclerosis (MS) presenting with pseudotumoral lesion (PTL) on MRI is a rare condition. We investigated the clinical presentations, radiological features and disability progression of PTMS in a North African population

Methods: Among the patients seen at our department (Razi hospital, Tunis) between 2005 and 2016, we identified cases of definite MS (McDonald 2010 criteria) showing a well-circumscribed T2 lesion with a diameter of > 2 cm. A total of 231 MS records were analysed using the local prospective MS database. We classified the lesions according to the recently proposed morphologic classification and the contrast enhancement pattern.

Results: Twenty-two patients (9.5%) (18 females, 4 males), mean age of 35.6 years [14-59], showed PTL. PTL at the onset of the disease were observed in 54.5%. All patients had a relapsing-remitting form. Ten patients (47.6%) had a polysymptomatic presentation at the disease onset. All PTL were supratentorial. Median largest lesion size was 32.4 mm [21-68]. The morphology of the largest PTL was categorized as being either Balo-like (n=2), megacystic (n=1), infiltrative (n=11) or ring-like (n=8). The contrast enhancement pattern was nodular (n=2), complete ring (n=1), incomplete ring (n=6) and diffuse (n=2). MR spectroscopy performed in four patients, showed an inflammatory profile. Annualized relapse rate was 0.7 and the mean final EDSS was 2.64. The mean progression index and MSSS were respectively 0.37 and 3.64.

Conclusion: Our findings showed a high frequency and a rather mild disease progression of PT forms of MS in our North African population.

Disclosure: Nothing to disclose

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EP3117

Cancelled

EP3118

Correlation between optical coherence tomography measures and visual evoked potentials in familial and sporadic MS patientsM. Siger¹, M. Grudziecka¹, K.W. Selmaj²¹Lodz, Poland, ²Łódź, Poland

Background and aims: The aim of this study was to find a correlation between the retinal nerve fiber layer (RNFL) thickness and macular volume (MV) measured by spectral-domain OCT (SD-OCT) with visual evoked potentials (VEP) in familial (fMS) and sporadic (sMS) multiple sclerosis patients.

Methods: 30 RR MS patients (17 fMS and 13 sMS) were recruited in the study. Both MS groups were matched according to disability measured by EDSS, annual relapse rate and disease duration. All patients had SD- OCT examination (Spectralis, Heidelberg Engineering) and VEP. Total RNFL thickness, MV, latency and amplitude of VEP were assessed in right and left eyes and were expressed as a mean value for both eyes for each patients

Results: Mean RNFL thickness in fMS were lower but not significantly than in sMS (91.5 ± 10.4 vs 93.03 ± 14.8 $p=0.1$). Mean MV in fMS did not differ from sMS (8.5 ± 0.5 vs 8.62 ± 0.4 $p=0.3$). Mean VEP latency was slightly longer, but not significantly, in fMS compared to sMS (120.40 ± 18.9 vs 116.7 ± 10.6 $p=0.1$). We observed a trend of lower mean VEP amplitude in sMS compared to fMS (8.64 ± 4.15 vs 11.84 ± 5.09 $p=0.06$). In fMS, but not in sMS, we found a modest correlation between mean RNFL and VEP latency ($r=-0.5$, $p=0.02$). In fMS we have also found modest a correlation between mean MV and VEP latency ($r=-0.4$, $p=0.04$).

Conclusion: Our results suggest that in fMS there is stronger correlation between structural retinal changes measured by OCT and visual system function measured by VEPs than in sMS patients.

Disclosure: Nothing to disclose

EP3119

Russian cohort of patients with NMO spectrum disorders: 58 casesT. Simaniv¹, I. Bakulin¹, E. Zhironova², M. Zakharova¹¹Research Center of Neurology, Moscow, Russian²I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation

Background and aims: Antibodies to aquaporin-4 (AQP4-Ab) is a sensitive and highly specific serum marker of neuromyelitis optica (NMO) and NMO-spectrum disorders (NMOSD). The aim of our research was to analyze the characteristics of patients with NMOSD according to demographics, clinical symptoms and MRI findings and estimate frequency of AQP4-Ab in Russian group patients with NMOSD.

Methods: Serum samples from 58 patients with NMOSD were analyzed. We used cell-based assay for the detection of AQP4-Ab (Euroimmun).

Results: 58 patients (81% female) aged 16-65 years (mean age 40.2 years) were included in the study. AQP4-Ab were detectable in 86.7% patients with NMOSD. The mean age of onset of symptoms was 38.4 years. The mean time to diagnosis was 16.9 months (range: 1 month-5 years). In most patients, the onset symptoms were longitudinally extensive transverse myelitis (LETM) and optic neuritis (ON) (62% and 34%, respectively). In three cases, the disease manifested with area postrema syndrome. In total, during disease course 6 patients developed area postrema syndrome, 2 – acute brainstem syndrome, and 2 – symptomatic cerebral syndrome. According to MRI, 83% of the 58 patients had LETM lesions and 14% had short transverse myelitis lesions extending fewer than three vertebral segments. Spinal cord lesions spanned 1-13 vertebral segments (mean 5.5). The cervical cord was involved in 30% of cases, thoracic cord – in 30%, both cervical and thoracic cord – in 40%. 19% of patients had brain lesions.

Conclusion: Our results confirm high clinical heterogeneity of NMOSD and specificity of AQP4-Ab as a marker of NMOSD.

Disclosure: Nothing to disclose

EP3120

Absolute lymphocyte counts in patients with relapsing multiple sclerosis (RMS) treated with cladribine tablets 3.5 mg/kg in the CLARITY and CLARITY Extension studies

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Background and aims: In CLARITY, the most commonly reported adverse event was lymphopenia, consistent with the mechanism of action for cladribine tablets (CT). We investigate the absolute lymphocyte count (ALC) in patients with RMS receiving 2 year’s treatment with CT 3.5mg/kg (CT3.5).

Methods: Data from patients randomised to CT3.5 for 2 years in CLARITY/CLARITY Extension including time spent in the PREMIERE registry (N=685) were pooled to provide long-term follow-up data. Data from patients randomised to placebo in CLARITY and followed up in CLARITY Extension and PREMIERE are also reported (PBO;N=435).

Results: At baseline (start of CLARITY or CLARITY Extension), median ALC was 1.86×10⁹/L for CT3.5 and 1.91×10⁹/L for PBO (Table). During Year 1, ALC in CT3.5 reached a nadir at 9 weeks post-treatment (1.00×10⁹/L;Figure). At the end of Year 1 (48 weeks), median ALC had increased to 1.21×10⁹/L. During Year 2, ALC in CT3.5 reached a nadir 7 weeks after re-treatment (0.81×10⁹/L), increasing to 1.03×10⁹/L at the end of Year 2 (96 weeks). At the end of Years 3 and 4 (144 and 192 weeks), ALC in the CT3.5 group (with no further treatment) increased to 1.36×10⁹/L and 1.40×10⁹/L, respectively, reaching a final median ALC of 1.76×10⁹/L after 6.5 years (312 weeks). In PBO patients, median ALC values were between 1.69×10⁹/L and 1.95×10⁹/L (Figure).

Figure. Median absolute lymphocyte counts over time in patients treated with cladribine tablets 3.5 mg/kg for 2 years or placebo: pooled data from CLARITY, CLARITY Extension and PREMIERE

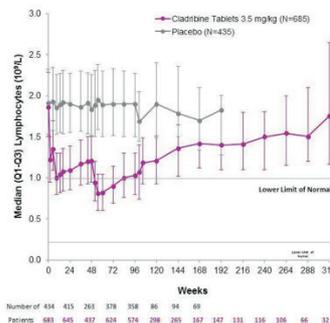


Figure 1

Conclusion: Rapid reductions in ALC after CT3.5 treatment in Years 1 and 2 were followed by gradual returns toward baseline. Median lymphocyte counts were within normal range beyond Year 2 (96 weeks) in all patients for whom follow-up data are available.

Disclosure: This study was funded by Merck KGaA, Darmstadt, Germany. Medical writing assistance was provided by inScience Communications, Springer Healthcare, Chester, UK, and was funded by Merck KGaA, Darmstadt, Germany.

Table. Median absolute lymphocyte counts in patients treated with cladribine tablets 3.5 mg/kg for 2 years or placebo: pooled data from CLARITY, CLARITY Extension and PREMIERE

Time point	Placebo (N=435*)	Cladribine tablets 3.5 mg/kg (N=685*)
Baseline	1.91×10 ⁹ /L (1.54-2.32)	1.86×10 ⁹ /L (1.50-2.29)
Year 1 (48 weeks)	1.84×10 ⁹ /L (1.52-2.24)	1.21×10 ⁹ /L (0.95-1.50)
Year 2 (96 weeks)	1.90×10 ⁹ /L (1.50-2.27)	1.03×10 ⁹ /L (0.80-1.30)
Year 3 (144 weeks)	1.79×10 ⁹ /L (1.50-2.34)	1.36×10 ⁹ /L (1.02-1.65)
Year 4 (192 weeks)	1.85×10 ⁹ /L (1.28-2.01)	1.40×10 ⁹ /L (1.10-1.81)
Year 5 (240 weeks)	1.89×10 ⁹ /L (1.18-2.74)	1.50×10 ⁹ /L (1.10-1.81)
Year 6.5 (312 weeks)	1.70×10 ⁹ /L (1.30-2.00)	1.76×10 ⁹ /L (1.17-2.45)

Data are median (Q1-Q3).
*Patient numbers decreased over time and are reported in Figure.

Table 1

EP3121

3T FLAIR* MRI evaluation of three lesions for central vessel sign demonstrates specificity for multiple sclerosis

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Background and aims: Multiple sclerosis (MS) diagnosis remains challenging due to reliance on radiographic assessments of imperfect specificity. FLAIR* MRI studies have demonstrated that detection of a “central vessel sign” (CVS) in MS lesions differentiates MS from other disorders. These studies have primarily evaluated identification of central veins in all MRI lesions, a method impractical for clinical application. This study evaluated the specificity and sensitivity of a limited assessment of CVS in only three lesions for MS diagnosis.

Methods: 40 participants were studied: 10 with MS without additional comorbidities for white matter abnormalities; 10 with MS with additional comorbidities for white matter abnormalities; 10 with migraine, MRI white matter abnormalities, and no additional comorbidities for white matter abnormalities; and 10 erroneously diagnosed with MS. 3T MRIs, performed with gadopentetate dimeglumine, were de-identified and randomly ordered and then provided to three MS physicians at three different institutions blinded to diagnosis. Three ovoid lesions 3mm³ in at least one plane and restricted to the subcortical or deep white matter were first selected in each patient on FLAIR and subsequently evaluated for CVS using FLAIR*.

Results: Two MS participants were excluded from analysis due to inadequate candidate lesions. Using a threshold of 3/3 lesions with CVS as diagnostic of MS resulted in mean specificity and sensitivity across readers of 0.98 and 0.52 respectively. With a threshold of 2/3 lesions, the corresponding values were 0.95 and 0.81.

Conclusion: Evaluation of only three lesions for CVS, using FLAIR* MRI, demonstrated high specificity and good sensitivity for MS.

Disclosure: Supported by the University of Vermont Department of Neurological Sciences, University of Vermont Department of Radiology, and the University of Vermont MRI Center for Biomedical Imaging, and partially supported by the Intramural Research Program of National Institute of Neurological Disorders and Stroke.

EP3122

Selective and discontinuous reduction of B and T lymphocytes by cladribine tablets in patients with early and relapsing multiple sclerosis (ORACLE-MS, CLARITY and CLARITY Extension)

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Background and aims: Efficacy of cladribine tablets (CT) 3.5mg/kg has been demonstrated in patients with early MS (ORACLE-MS) and in patients with relapsing multiple sclerosis (RMS) in CLARITY/CLARITY Extension studies.

Methods: Longitudinal (48 weeks) evaluation of peripheral blood lymphocyte subtypes from patients treated with CT 3.5mg/kg (N=274) or placebo (N=140) was conducted. CLARITY Extension patients received placebo in CLARITY and switched to CT 3.5mg/kg in the Extension phase. Lymphocytes were measured at baseline, and Weeks 5, 13, 24 and 48. Changes in absolute counts and changes in relative proportion of the lymphocyte subtypes were evaluated.

Results: The baseline distributions of absolute lymphocyte counts (ALC) were similar across studies. Profiles of CD19+ B lymphocytes and CD4+ and CD8+ T lymphocytes were generally consistent across studies. The most rapid reduction in cell numbers occurred in the CD19+ B cell compartment (approximately 75% at Week 5 in each study). Nadir was reached at Week 13 with >80% reduction, and reconstitution towards baseline occurred from Week 24 to 48. CD4+ and CD8+ T cells were also markedly reduced in numbers, but to a lesser degree than CD19+ B cells (at most 55%; ORACLE-MS). Cladribine had a stronger suppressive effect on CD4+ than CD8+ T cells. There was only incomplete reconstitution of T cells at Week 48. Changes in relative proportion confirmed the effect on CD19+ B cells at ALC nadir.

Table Lymphocyte profiles up to Week 48 in CLARITY, CLARITY Extension and ORACLE			
Median percent change from baseline in absolute counts	CD19+ B cells Week 5/13/24/48	CD4+ T cells Week 5/13/24/48	CD8+ T cells Week 5/13/24/48
Placebo CLARITY (N=93)	1/2/3/4	-4/-1/0/-3	2/1/2/5
3.5 mg/kg CLARITY (N=97)	-75/-81/-64/-34	-23/-48/-46/-43	-21/-35/-29/-30
3.5 mg/kg CLARITY EXT (PP1) (N=136)	-74/-84/-67/-32	-24/-50/-49/-43	-20/-29/-36/-33
Placebo ORACLE (N=47)	5/0/17/19	5/5/10/15	14/6/6/-3
3.5 mg/kg ORACLE (N=41)	-75/-82/-61/-34	-23/-55/-53/-51	-17/-44/-47/-48

Table 1

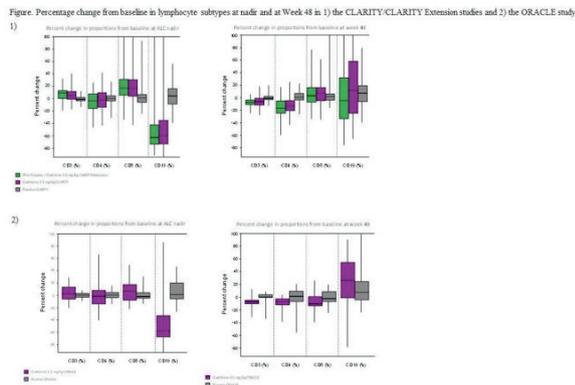


Figure 1

Conclusion: CT3.5 mg/kg achieved an early and discontinuous reduction of peripheral blood B cells with a rapid reconstitution to baseline, and a moderate reduction in T cell counts.

Disclosure: This study was funded by Merck KGaA, Darmstadt, Germany. Medical writing assistance was provided by inScience Communications, Springer Healthcare, Chester, UK, and was funded by Merck KGaA, Darmstadt, Germany.

EP3123

Levels of serum anti-Müllerian hormone in women with early stage of relapsing-remitting multiple sclerosis

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Background and aims: Multiple sclerosis (MS) is a neurological disease mostly affecting women of childbearing age. Recent studies suggest that MS may have a negative impact on fertility. Decreased ovarian reserve is supposed to be one of the most important factors for fertility impairment. It is not known if ovarian decline contributes to accumulation of disability in women with MS when evaluated using EDSS. Anti-Müllerian hormone (AMH) represents a measure of ovarian reserve unrelated to the menstrual cycle. The purpose of this study was to determine AMH levels in females with relapsing-remitting MS (RRMS) in comparison with healthy volunteers.

Methods: A total of 104 reproductive-age females (mean age 34.1±6.1, median EDSS 2.5) with RRMS and 77 age matched healthy controls (mean age 32.1±5.7) were included. An enzymatically amplified two-site immunoassay was used to measure serum AMH level.

Results: Mean AMH levels were similar in females with RRMS (2.78 ng/ml) and healthy controls (3.11 ng/ml) (p=0.31). However, on individual level, 9 MS patients (8.6%) showed very low AMH values (<0.4 ng/ml) compared 2 healthy controls (3%) (p<0.01). AMH levels were not associated with EDSS values (Pearson coefficient 0.23, p=0.05).

Conclusion: On the group level, no reduction of follicular reserve was found in women with MS. On individual level, however, higher proportion of women with very low AMH values was found in MS group comparing to healthy controls. These results suggest possible negative impact of MS disease on fertility of some of the patients.

Disclosure: Nothing to disclose

EP3124

Free radical pathology in early progression of multiple sclerosis

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Background and aims: Several factors can compromise the endogenous protective system of organism and accelerate the induction of free radicals that may influence the course of MS.

Study aimed to investigate the role of several possible risk factors in secondary progression of MS.

Methods: We investigated smoking, dietary patterns, alcohol intake, severe and chronic stress in 60 secondary progressive MS (SPMS) patients, 33 (first group) from refugees, 27 from general population (second group). Age at disease onset, disease duration, number of relapses, length of period until the secondary progression of disease and the Kurtzke Expanded Disability Status Scale (EDSS) scores were collected. Control comprised 15 healthy volunteers. Brain was visualized by Magnetic Resonance Tomography (MRT-1.5-Tesla). Mood examined by Beck Depression Inventory (BDI-II). Blood free radicals detected by Electron Paramagnetic Resonance Method (EPR). Statistics was performed by SPSS-11.0

Results: First group developed SPMS in a shorter period compared to second group (7.2 ± 2.1 versus 16.4 ± 3.8 , $p < 0.05$). Multiple logistic regression found the significance of smoking and depression for development of SPMS ($p < 0.05$). Depression was found in 85% of first - and in 23% of second group ($BDI > 9/10$). Lypoperoxyradical (LOO-) and superoxide anion (O₂-) were increased in first group as compared to second group and control. Positive correlation was established between BDI index and LOO- and O₂- data ($r = +0.33$ and $r = +0.19$, $p < 0.05$)

Conclusion: Smoking and depression due to chronic social stress may contribute to the promotion of free radical pathology in MS and thus, can stimulate the neurodegeneration.

Disclosure: Nothing to disclose

EP3125

The NLRP1 and NLRP3 inflammasomes are activated in multiple sclerosis and clinically isolated syndrome

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Background and aims: Inflammasome is a multiprotein oligomer expressed in myeloid cells and involved in inflammatory processes. In this study, we aimed to analyze the value of serum and cerebrospinal fluid (CSF) levels of NLRP1 and NLRP3 inflammasomes as predictors of conversion to multiple sclerosis (MS).

Methods: A total of 23 relapsing remitting MS (RRMS) patients, 18 clinically isolated syndrome (CIS) patients and 30 healthy controls were recruited for this study. Patients were in remission and were not under immunosuppressive treatment during serum and CSF sampling. Disease durations, EDSS scores, relapse numbers and oligoclonal band (OCB) status of all patients were recorded. Serum and CSF levels of NLRP1 and NLRP3 were measured using ELISA.

Results: While both RRMS and CIS patients had significantly higher serum and CSF levels of NLRP1 and NLRP3 than healthy controls, there were no significant differences between MS/CIS patients and healthy controls. Moreover, CSF but not serum levels of OCB positive patients were significantly higher than those of the OCB negative patients. There were no correlations between NLRP1/NLRP3 levels and clinical-demographic features of MS patients.

Conclusion: Inflammasome complex appears to be activated as early as during the first MS attack. However, levels of NLRP1 and NLRP3 are not altered in a time- or disability-dependent manner and thus cannot be used as indicators of MS conversion or as a prognostic biomarker. Increased CSF NLRP1/NLRP3 levels of OCB positive patients might indicate enhanced blood-brain barrier transport of myeloid cells in these patients.

Disclosure: Nothing to disclose

EP3126

Prognostic value of adipokines in multiple sclerosis

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Background and aims: Adipokines are known to be involved in numerous inflammatory diseases. This study aimed to analyze the value of serum adipokine levels as biomarkers in determining the clinical progression of multiple sclerosis (MS).

Methods: A total of 50 MS patients and 40 healthy individuals were recruited for this study. Clinical course of MS patients was classified as benign (>10 years of disease duration and ≤ 3 EDSS score) and classical (>10 years of disease duration and >3 EDSS score). Disease duration, annual relapse rate, EDSS and attack types of MS patients were recorded. Levels of serum adipokines and adipocyte-derived cytokines were measured using ELISA.

Results: Serum adiponectin, monocyte chemoattractant protein 1 (MCP-1), TNF- α and IL-6 levels were significantly higher in classical MS patients than benign MS patients and healthy controls. There were no significant differences between levels of leptin, resistin, IL-1 β and IL-8 among groups. Adiponectin, MCP-1 and TNF- α levels were directly correlated with EDSS scores. Notably, MS patients with an initial attack of optic neuritis displayed significantly lower EDSS scores, adiponectin, MCP-1 and TNF- α levels than other MS patients. There was no correlation between adipokine levels and other clinical-demographic features.

Conclusion: Adipokines appear to be involved in clinical progression of MS and thus adiponectin, MCP-1 and TNF- α might potentially serve as prognostic biomarkers in MS. Our results confirm previous studies which have claimed that MS initiating with optic neuritis has a relatively more benign course.

Disclosure: Nothing to disclose

EP3127

The effect of delayed-release dimethyl fumarate on lymphocyte subsets and immunoglobulins in patients with relapsing-remitting multiple sclerosis: Interim results of an open-label phase 3 study

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Background and aims: Delayed-release dimethyl fumarate (DMF, also known as gastro-resistant DMF) is a twice-daily (BID) oral medication approved for the treatment of relapsing-remitting multiple sclerosis (RRMS). In an integrated analysis of the DMF pivotal trials, the mean absolute lymphocyte count (ALC) decreased by ~30% in the first year of treatment and then stabilized, remaining above the lower limit of normal. This ongoing study (NCT02525874) evaluates the effect of DMF on lymphocyte subset counts and immunoglobulins during the first year of treatment in patients with RRMS.

Methods: This ongoing, open-label, multicenter, phase 3 study enrolled and treated (DMF, 240 mg BID) 218 patients diagnosed with RRMS aged 18-65 years. Blood samples were collected at screening, day 1, and at weeks 4, 8, 12, 24, 36, and 48. Changes in lymphocyte subsets were evaluated using a comprehensive panel of cell surface markers and intracellular cytokines by flow cytometry.

Results: Of the 218 enrolled patients, 163 patients had ≥ 6 months follow-up or had discontinued the study earlier and were included in this interim analysis. Detailed phenotypic characterizations of CD4⁺, CD8⁺, B, and natural killer cell subsets, changes in ALCs, and incidence of adverse events will be presented.

Conclusion: Interim data from this study will provide further understanding of how DMF influences immune cell subsets in the first 6 months of treatment and how those changes correlate with changes in ALCs.

Disclosure: CVH, DM, CP, LY, SL, and SIS are full-time employees of and hold stock/stock options in Biogen. SR performed the majority of the work while an employee of Biogen, Cambridge, MA.

EP3128

Durable clinical and MRI efficacy of Alemtuzumab over 6 years in CARE-MS I patients with active RRMS with relapse between courses 1 and 2

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Background and aims: Alemtuzumab 12 mg/day (baseline: 5 days; 12 months later: 3 days) improved 2-year outcomes versus SC IFNB-1a in treatment-naïve patients with active relapsing-remitting MS (RRMS) (CARE-MS I; NCT00530348), with durable efficacy through 6 years (NCT00930553). 85% of alemtuzumab-treated patients were relapse-free between Courses 1–2. We evaluated 6-year efficacy in patients who relapsed in this interval.

Methods: Assessments: annualised relapse rate (ARR); freedom from 6-month confirmed disability worsening (CDW), MRI disease activity (gadolinium [Gd]-enhancing T1 and new/enlarging T2 lesions), or new T1 hypointense lesions; brain volume loss (BVL).

Results: 56/376 (15%) alemtuzumab-treated patients relapsed between Courses 1–2; 52/56 (93%) enrolled in extension; 45/52 (87%) remained through Year 6. In patients who relapsed, ARR in Year 1 (1.3) declined in the year after Course 2 (0.3); 27% relapsed in Year 2. ARR remained 0.3–0.5 over Years 3–6. 60% of patients remained 6-month CDW-free through Year 6. Most were free of Gd-enhancing T1 lesions (84%), new/enlarging T2 lesions (71%), MRI disease activity (69%), and new T1 hypointense lesions (90%) in Year 6. Median percent yearly BVL declined over time: Years 1–6: –0.67%, –0.17%, –0.20%, –0.11%, –0.21%, –0.24%. 46% of patients received ≥1 alemtuzumab retreatment.

Conclusion: Outcomes during Year 1 of alemtuzumab do not predict longer-term response. Patients who relapsed in Year 1 improved markedly in subsequent years. These data support administering alemtuzumab according to approved labeling (2 courses) for optimal and durable clinical/MRI benefits in the small population of patients experiencing relapse between Courses 1–2.

Disclosure: Sanofi and Bayer HealthCare Pharmaceuticals.

EP3129

Real world studies of glatiramer acetate: Differences of MS patient profiles between 2 non-interventional studies COPTIVITY and QualiCOP

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Background and aims: The MS treatment landscape has changed rapidly. With the approval of DMTs new first and second-line treatment options for RRMS became available. QualiCOP and COPTIVITY are two independent non-interventional studies (NIS) with glatiramer acetate (GA), representing an area before and after oral DMTs were approved. We aimed to determine if prior treatment with oral DMTs impact the treatment algorithm with GA and patients' treatment decision.

Methods: QualiCOP (n=754) was a prospective, observational, open-label NIS (recruitment Aug. 2007 - May 2009). COPTIVITY (n=969, interim analysis) is an ongoing two-year, multicentre, open-label NIS (recruitment Dec. 2014 - Mar. 2016).

Results: Baseline characteristics were comparable (mean age 39.4 vs. 38.6 years, 78.9% vs. 73.0% female, stable MS 39.5% vs. 34.0%). In COPTIVITY, patients were characterized by shorter disease duration (3.9 vs. 4.7 years), lower relapse rate (1.2 vs. 1.8 relapses), and a lower mean EDSS (2.0 vs. 2.3) compared to QualiCOP patients. In COPTIVITY, 15.1% of patients switched from a variety of DMTs (e.g. 7.5% fingolimod, 9% teriflunomide, 33.1% dimethylfumarate, and 66.9% IFN-beta drugs) compared to QualiCOP (31% IFN-beta drugs). Increasingly more patients using the new three-times-weekly 40 mg GA formulation.

Conclusion: Pre-treated patients in the recent COPTIVITY had undergone a greater variety of MS treatment before GA, reflecting the approval of new DMTs. Even though new oral DMTs are available these results emphasize the importance of GA as a platform therapy in RRMS.

Disclosure: This study is funded by TEVA GmbH Germany, Berlin.

Neurogenetics

EP3130

Digenic causes to Charcot-Marie-Tooth disease in two families

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Background and aims: Next-generation sequencing (NGS) or massively parallel sequencing detects the precise order of nucleotides within a DNA molecule. NGS is more effective than traditional sequencing methods, such as Sanger sequencing, when several genes are involved. Targeted NGS is starting to be used in diagnostics for disorders caused by several genes. About 100 genes may cause hereditary neuropathies. Charcot-Marie-Tooth disease (CMT) is the most frequent hereditary neuropathy with a prevalence of 40-80 per 100,000 in Norway. It is probable that some patients has mutations in more than one gene causing the phenotype.

Methods: CMT patients from two families were investigated for PMP22 duplications and point mutations in CMT genes with the methods Multiplex Ligation-dependent Probe Amplification (MLPA) and NGS.

Results: We identified a digenic cause to CMT in the two families, i.e. in the first family a duplication of PMP22 together with a compound heterozygous SH3TC2 mutation and in the other family point mutations in the genes PMP22 and NEFL.

Conclusion: If the phenotype is atypical or more severe than expected may be worthwhile to investigate selected CMT patients for more than one genetic cause to their phenotype. The pedigree may sometimes indicate a digenic cause to the overall phenotype of CMT patients. Digenic causes to CMT may be more frequent than previously anticipated – 1-2%.

Disclosure: Nothing to disclose

EP3131

The different faces of the p.A53T alpha-synuclein mutation: A screening of Greek patients with parkinsonism and/or dementia

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Background and aims: The p.A53T mutation in the alpha-synuclein (SNCA) gene is a rare cause of autosomal dominant Parkinson's disease (PD). Although generally rare, it is particularly common in the Greek population due to a founder effect. A53T-positive PD patients often develop dementia during disease course and may very rarely present with dementia.

Methods: We screened for the p. A53T SNCA mutation a total of 347 cases of Greek origin with parkinsonism and/or dementia, collected over 15 years at the Neurogenetics Unit, Eginition Hospital, University of Athens. Cases were classified into: "pure parkinsonism" (PD, atypical parkinsonism), "pure dementia" (frontotemporal dementia, Alzheimer disease, "other") and "parkinsonism plus dementia" (frontotemporal dementia with parkinsonism, PD dementia, Lewy Body disease, atypical parkinsonism).

Results: In total, 4 p.A53T SNCA mutation carriers were identified. All had autosomal dominant family history and early onset. Screening of the "pure parkinsonism" category (137 cases) revealed 2 cases with typical PD. The other two mutation carriers were identified in the "parkinsonism plus dementia" category (89 cases). One had a diagnosis of PD dementia and the other of behavioral variant frontotemporal dementia. Screening of patients with "pure dementia" (121 cases) failed to identify any further A53T-positive cases.

Conclusion: Our results confirm that the p.A53T SNCA mutation is relatively common in Greek patients with PD or PD plus dementia, particularly in cases with early onset and autosomal dominant family history. However, routine screening of patients with "pure dementia" is unlikely to be clinically useful even in the Greek population.

Disclosure: Nothing to disclose

EP3132

Gordon Holmes syndrome, one of the many faces of PNPLA6V. Carvalho¹, J. Martins²¹Porto, Portugal, ²Neurology, Hospital Pedro Hispano, Matosinhos, Portugal

Background and aims: The association of cerebellar ataxia and hypogonadism was first described by Holmes in 1907. Recently, PNPLA6-spectrum of neurodegenerative disorders has been described, with a clinical phenotype ranging from pure cerebellar ataxia to Oliver-McFarlane syndrome. Although many cases are of familiar aggregation, often with consanguinity history, sporadic cases have been reported.

Methods: A clinical case and review of literature.

Results: A 66-year-old male presented to our clinic with progressive gait impairment, which started when he was 16. Due to his past heavy drinking, his symptoms were initially thought to be of toxic etiology. His past medical history also included delayed puberty due to hypogonadotropic hypogonadism and diabetes mellitus type 2. He had no history of consanguinity nor significant family history. On physical examination, he presented gynecoid appearance with gynecomastia and on neurological examination he had moderate dysarthria, multidirectional nystagmus, axial and peripheral ataxia and unstable gait. He had no retinopathy. His diagnostic work-up, which included nutritional, paraneoplastic and microbiologic studies, was normal and the brain MRI showed marked cerebellar atrophy. Due to the clinical suspected Gordon Holmes' syndrome a search for mutations in RNF216 gene was performed with negative results. Afterwards, biallelic mutations to the PNPLA6 gene were found, confirming the diagnosis.

Conclusion: Several confounders can delay the diagnosis of cerebellar ataxias presenting in adulthood, and a progressive ataxia after removal of aggressors should always lead to the search of another etiology. The coexistence of two of ataxia, hypogonadism, motor neuron disease or chorioretinal dystrophy should raise suspicion of a PNPLA6 spectrum disorder.

Disclosure: Nothing to disclose

EP3133

Primary appearing tremor-dystonia, due to homozygous mutation p.V2716A in ATM gene in Bulgarian muslimsT. Chamova¹, D. Kancheva², T. Todorov³, I. Pacheva⁴, I. Ivanov⁴, S. Cherninkova¹, D. Zlatareva⁵, V. Hadjiiska⁶, E. Naumova⁷, A. Jordanova², A. Todorova⁸, I. Tournev⁹¹Department of Neurology, Sofia Medical University, University hospital "Alexandrovska", Sofia, Bulgaria, ²Molecular Neurogenomics Group, Department of Molecular Genetics, VIB; Neurogenetics Laboratory, Institute Born-Bunge, University of Antwerp, Antwerp, Belgium;³Department of Medical Chemistry and Biochemistry, Sofia, Bulgaria, ⁴Genetic Medico-Diagnostic Laboratory "Genica", Sofia, Bulgaria, ⁵Department of Pediatrics and Medical Genetics, Plovdiv Medical University, Plovdiv, Bulgaria, ⁶Department of Diagnostic Imaging, University Hospital "Alexandrovska", Medical University, Sofia, Bulgaria, ⁷Department of nuclear medicine, University Hospital "Alexandrovska", Medical University, ⁸Department of immunology, University Hospital "Alexandrovska", ⁹Department of Medical Chemistry and Biochemistry; Genetic Medico-Diagnostic Laboratory "Genica", ⁹Sofia Medical University, Department of Neurology, University Hospital Alexandrovska, Department of Cognitive Science and Psychology, New Bulgarian University, Sofia, Bulgaria

Background and aims: Ataxia-telangiectasia (A-T) is a rare autosomal recessive disorder due to mutations in the ATM-gene. The classical phenotype is characterized by progressive childhood-onset cerebellar ataxia, oculomotor apraxia, telangiectasias of the conjunctivae, hypersensitivity to ionizing radiation, and immunodeficiency. Recently some ATM mutations were found to manifest as generalized or focal dystonia without any of the classical signs of A-T.

The aim of the study is to evaluate the clinical features in a group of 14 Bulgarian patients, belonging to a religious minority, homozygous for V2716A in ATM-gene.

Methods: The study encompassed 14 patients, belonging to two big Bulgarian muslim pedigrees, with data of more than 25 affected from four consequent generations. All of them underwent neurological evaluation. Brain MRI was performed in 7, PET-CT- in 1, neuroophthalmological assessment- in 9. Exome sequencing was performed in 8- 5 affected and 3 healthy relatives.

Results: The age at onset in our group varies between 14 days and 20 years. The main symptoms are dystonic and choreic hyperkinesias, more prominent in the upper limbs and the neck, dystonic dysarthria and dysphagia. The clinical course was very slowly progressive. Brain imaging was normal. In all the affected a homozygous mutation p.V2716A in ATM gene was found.

Conclusion: Clinical features, due to mutations in ATM gene can be very broad. The disease may appear as dystonia, especially of early onset, without frank cerebellar involvement and also normal cerebral imaging. A-T should be considered in all patients with unexplained, even mild movement disorders.

Disclosure: Nothing to disclose

EP3134

Cancelled

EP3135

Early onset autonomic dysfunction with both sympathetic and parasympathetic involvement in Charcot-Marie-Tooth Disease type 2JA.E. Friis-Hansen¹, M. Ballegaard², I. Christiansen¹, K. Svenstrup¹¹Neuromuscular, Rigshospitalet, Copenhagen, Denmark,²Clinical Neurophysiology, Rigshospitalet, Copenhagen, Denmark

Background and aims: Charcot-Marie-Tooth type 2J (CMT2J) is an autosomal dominantly inherited axonal sensorimotor polyneuropathy caused by a few missense mutations in the MPZ gene. It is characterized by pupillary abnormalities, hearing loss, late onset sensorimotor polyneuropathy and parasympathetic autonomic dysfunction.

Methods: A Thr124Met MPZ mutation was found in a 52-year-old-male and his daughter. They presented at respectively 30 and 20 years of age with problems emptying the bladder and the daughter needed chronic intermittent catheterization at 24 years of age. The index patient underwent prostate resection and later developed erectile dysfunction. At 45 years of age he had onset of symptoms of sensory and motor symptoms in his feet. The patients underwent autonomic testing, nerve conduction studies (NCS), urodynamics in addition to neurological examination at 56 and 26 years of age, respectively.

Results: Clinical examination revealed tonic pupils in the daughter and clinical signs of CMT in the index patient. Autonomic testing of the daughter showed primarily sympathetic involvement, with an abnormal fall in pulse amplitude during Valsalva's maneuver and an abnormal heart rate increase during the head-up tilt, but minor abnormalities in the index patient. NCS showed an axonal sensorimotor polyneuropathy in the index patient and normal results in the daughter. Urodynamics showed hypotonic bladders and lack of sphincter relaxation.

Conclusion: We report clinical and paraclinical data on two patients with CMT2J. The data show a sympathetic dysfunction in CMT2J in addition to a parasympathetic involvement as previously reported. Autonomic symptoms precede classic polyneuropathy symptoms and can result in unnecessary surgery.

Disclosure: Nothing to disclose

EP3136

Neurological phenotype of Ataxia-Pancytopenia Syndrome caused by SAMD9L mutations in a Swedish familyS. Gorcenco¹, J. Davidsson², U. Tedgård³, D. Turkiewicz⁴, L. Nilsson⁵, C. Nilsson¹, J. Cammenga⁶, A. Puschnann¹¹Department of Clinical Sciences, Lund, Neurology, Sweden, Lund University, Skåne University Hospital, Lund, Sweden,²Division of Molecular Hematology, Institution for Laboratory Medicine and Department of PaediatricOncology and Hematology, Skåne University Hospital, Lund, Sweden, Lund University, Lund, Sweden, ³Department ofPaediatric Oncology and Hematology, Lund University, Skåne University Hospital, Lund, Sweden, ⁴Department ofPaediatric Oncology and Hematology, Lund University Hospital, Lund, Sweden, ⁵Division of Molecular Hematology,Institution for Laboratory Medicine, Lund University, Lund, Sweden, ⁶Division of Molecular Hematology, Institution for

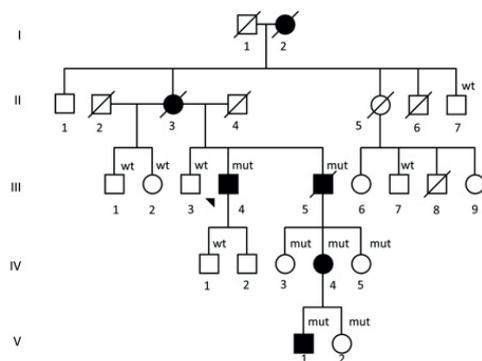
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Background and aims: Missense mutations in SAMD9L have recently been identified as the cause of autosomal dominant Ataxia-pancytopenia syndrome, with neurological features, hematologic cytopenias and markedly increased leukaemia risk. We recently reported a Swedish family with this syndrome and a SAMD9L c.2956C>T (p.Arg986Cys) mutation (Tesi et al. Blood 2017).

Methods: We expanded the pedigree, examined additional family members, reviewed charts and radiological examinations, compiling data on a total of 21 members. Genetic analysis was performed on buccal swabs.

Results: Six members of the family had neurological signs or symptoms. Age at onset varied from 6 to 15 years. The initial symptom was gait imbalance in all affected individuals. Symptoms were slowly progressive but remained generally mild. Two individuals had dysmetria and only one dysarthria. Additional signs were horizontal and vertical nystagmus, hyperreflexia and foot clonus. One family member, who received matched unrelated HSC transplantation at age 4.5 years because of myelodysplastic syndrome, displayed marked neurological deficit after cytostatic treatment. Neuroimaging revealed cerebellar atrophy and supratentorial white matter changes in all patients examined. Seven of 13 family members tested carried the SAMD9L c.2956C>T mutation. Three mutation carriers have not been examined yet. For five mutation carriers a history of cytopenia was confirmed, but it may have been intermittent and mild.



Family tree

Neurologic evaluation of patients with germline SAMD9L c.2956C>T mutations

Individual	Onset of neurological symptoms	Current Age	Balance impairment	Nystagmus	Deep Tendon Reflexes	Dysmetria	Dysarthria	Cerebellar atrophy	White matter lesions
I-2	NA	00†	Mild	NE	NE	NE	NE	NE	NE
II-3	NA	87†	Moderate to severe	NE	NE	+	+	Marked	Marked
III-4	15 years	64	Mild	Horizontal and vertical	Brisk	-	-	Marked	Moderate periventricular
III-5	NA	58†	Very mild	NE	NE	NE	NE	NE	NE
IV-4	Insidious onset in childhood	33	Very mild	Horizontal and vertical	Brisk	-	-	NE	NE
V-1	6 years	6	Severe to moderate	Vertical	Brisk	+	-	Marked	Marked

NE: not examined; NA: not applicable; +: present; -: absent; †: individual deceased, age at death. Individuals IV-3, IV-5 and V-2 are known mutation carriers but have not been examined yet at the time of abstract submission.

Neurologic evaluation of patients with germline SAMD9L c.2956C>T mutations

Conclusion: The neurological phenotype of patients with SAMD9L mutation includes slowly progressive gait imbalance and nystagmus which often remain disproportionately mild compared to marked cerebellar atrophy on imaging. Testing for SAMD9L mutations should be performed on non-hematopoietic tissue due to mosaicism in blood.

Disclosure: Institutional support for this research has been granted by ALF, MultiPark, Lund University and Skåne University Hospital, Sweden.

EP3137
Cancelled

EP3138
Cancelled

EP3139
The AARS-related neuropathy in four Czech patients – clinical and electrophysiological study

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Background and aims: Mutations in genes encoding aminoacyl-tRNA synthetases (ARS) cause several forms of CMT2 with different clinical and electrophysiological features. In four CMT2 patients (3M + 1F) from one large family we found causative mutation c.986G>A (p. Arg329His) in heterozygous state in the AARS gene (alanyl t-RNA synthetase) (AARS).

Methods: The onset of disease ranged between age 10-18y, first symptoms were symmetrical weakness and atrophies of peroneal and calf muscles. Neurological exams were performed at different ages of patients (35F, 40M, 52M, 59M). We found mild pes cavus, severe peroneal and calf muscle atrophies drop and steppage gait. The sensory symptoms included deficit of vibration and touch at LL, except of a 35y old female.

Results: EDX studies confirmed intermediate conduction abnormalities on motor fibers at UL and no responses at LL. Sensory fibers of median nerve were excitable with low amplitude of SNAP, conduction slowing at wrist and no responses of sural nerve in all patients. The conduction studies confirmed mixed demyelinating and axonal lesion in all patients.

Conclusion: The phenotype of our patients was similar. The clinical neuropathic symptoms at the onset were mostly motor and less sensory in symmetric distribution at LL and mimic distal motor neuropathy. The paraparesis of LL started during second decade and has a relatively slow progression, two patients were able to walk without support at age over fifty. Electrophysiological studies confirmed a mixed demyelinating and axonal lesion of motor and sensory nerve fibers at the onset of the disease and distinguish CMT2N from distal motor neuropathy.

Disclosure: Nothing to disclose

EP3140

APOE haplotypes modify the associations of the ACE insertion/deletion polymorphism with neuropsychiatric symptoms in dementia due to Alzheimer's disease

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Background and aims: Associations of the insertion allele of an Alu repeat insertion/deletion (I/D) polymorphism in intron 16 of ACE with dementia due to Alzheimer's disease (AD) are not consistent in all studies. We sought to examine associations of APOE haplotypes and the ACE I/D polymorphism with neuropsychiatric symptoms according to each stage of AD.

Methods: In this cross-sectional study, participants with AD according to National Institute on Aging – Alzheimer's Association criteria were screened with the Clinical Dementia Rating and the 10-item Neuropsychiatric Inventory. Genotyping was undertaken with TaqMan® Real-Time Polymerase Chain Reactions for rs7412 and rs429358 (APOE haplotypes), and with Polymerase Chain Reactions for the ACE I/D polymorphism. After stratification by APOE-ε4 carrier status, the ACE I/D polymorphism was correlated with neuropsychiatric symptom scores in each dementia stage by way of a linear regression model with and without adjustment for therapy with psychotropic drugs and angiotensin-converting enzyme inhibitors, significance at $p < 0.05$.

Results: Among 207 consecutive outpatients, 108 (52.2%) were APOE-ε4 carriers and 99 (47.8%) were APOE-ε4 non-carriers; mean age at dementia onset was 73.27 ± 6.7 years-old for 140 females (67.6%) and 67 males (32.4%). The ACE I/D polymorphism was in Hardy-Weinberg equilibrium ($p = 0.37$). Considering mildly impaired patients, the insertion allele of ACE was cumulatively associated with agitation only for APOE-ε4 carriers in the unadjusted model ($\beta = 1.710$; $p = 0.042$), and with apathy only for APOE-ε4 non-carriers both in the unadjusted ($\beta = 1.682$; $p = 0.036$) and the adjusted ($\beta = 1.759$; $p = 0.035$) models.

Conclusion: Associations of the insertion allele of ACE with neuropsychiatric symptoms of mildly impaired patients with AD depend upon APOE haplotypes.

Disclosure: Supported by grant #2015/10109-5, The State of São Paulo Research Foundation (FAPESP).

EP3141

Clinical exome sequencing in muscular disorders

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Background and aims: Muscular disorders are characterized by clinical and genetic heterogeneity. There is no widespread consensus for clinical indications for next generations sequencing (NGS) nor standardized NGS methodological approaches. Our aim is to present the experience of systematic use of NGS in clinical diagnostics of muscular disorders.

Methods: Clinical indication for NGS testing in the period from 2014-2016 was a high risk for inherited muscular disorder, based on the history of disease, symptoms and signs as well as positive and negative characteristics of clinical diagnostic workup. NGS was performed using TruSight One (4813 genes) or whole exomes sequencing approaches followed by sequencing on HiSeq 2500 or MySeq platforms (Illumina). Interpretation of variants was done using in-house developed bioinformatic protocol.

Results: 50 patients with muscular disorders were offered NGS including 12 (24%) pediatric cases. 20% of patients had family history of disease. The largest group (52%) were patients with unspecific diagnosis of muscular disease, followed by congenital myopathies (26%), limb girdle muscular dystrophies and (12%), congenital myotonias (6%) and dystrophies (4%). Diagnostic yield was 62%; a high diagnostic rate of 69% was present in patients with unspecific diagnosis and 84% among pediatric patients. Average time to diagnosis was 17.7 years. We found pathologic gene variants in 21 genes and one pathologic CNV.

Conclusion: NGS proved to be a highly efficient diagnostic tool, especially in pediatric period and in patients with unspecific diagnosis of a muscular disorder.

Disclosure: Nothing to disclose

EP3142

A family with autosomal dominant late onset-Alexander disease, due to c.209G>A p.R70Q mutation in GFAP

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Background and aims: Alexander disease (AD) is a rare neurodegenerative disorder caused by mutations in the gene encoding glial fibrillary acidic protein (GFAP). AD is classified into three main forms: Infantile, juvenile and adult. Adult onset (AOAD) commonly presents with bulbar and pseudobulbar symptoms. Spastic paraparesis, urinary disturbances, ataxia, palatal myoclonus and dysautonomia have also been reported. We describe a family with four affected from three generations.

Methods: Whole exome sequencing (WES) was conducted on 10 family members. They underwent physical, neurological, neuropsychological examinations, cerebral magnetic resonance imaging (MRI), electromyography (EMG) and evoked potential (EP) testing.

Results: WES detected a missense heterozygous mutation (c.209G>A p.R70Q) in exon 1 of the GFAP gene in 5 individuals, four of whom were symptomatic and one still asymptomatic at age 28. The clinical onset varied from 15-25 years, presenting with ataxia, dysphagia, dysarthria, dysphonia, orofacial dystonia, lower spastic paraparesis, disturbed proprioception and paresthesia in the lower limbs, urinary incontinency and mild to severe cognitive decline. Two affected from the first and second generations died at ages 50 and 46 respectively. Brain and spinal cord MRI revealed confluent, symmetric white matter abnormalities in all cerebral lobes and atrophy of the cerebellum, medulla and upper cervical spinal cord. EMG was consistent with axonal polyneuropathy in the lower limbs; also EPs were abnormal.

Conclusion: We observe a wide interfamilial phenotypical variability in relation to disease onset and clinical severity, with no correlation between the two. The extensively distributed leucoencephalopathy and axonal polyneuropathy observed in our family are atypical to AOAD.

Disclosure: Nothing to disclose

EP3143

Association of BDNF Val66Met polymorphic variant with cognitive impairment in Parkinson's disease

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Background and aims: An association between Val66Met brain-derived neurotrophic factor (BDNF) polymorphism and Parkinson's disease (PD) has been disproved in the large meta-analysis of 15 studies. However, Val66Met BDNF polymorphism, resulting in abnormal intracellular distribution and low activity-dependent secretion of BDNF, has been associated with cognitive dysfunctions in PD patients in several studies. Our aim is to evaluate the impact of Val66Met BDNF polymorphic variant on cognitive functions in PD patients.

Methods: 200 patients and 150 ethnically, age and sex-matched controls without neurological disorders were included in the study. Genotyping was carried out by tetra-primer amplified refractory mutation system (ARMS)-PCR. We performed the cognitive examination in 105 patients with PD (62 PD patients with cognitive impairment and 43 without cognitive impairment). Cognitive functions were tested using mini-mental state examination (MMSE), Montreal Cognitive Assessment (MoCA), verbal fluency test, and clock-drawing test.

Table 1. Neuropsychological assessment of PD patients.

Test	66Met BDNF carriers*	Val/Val BDNF carriers*
MMSE	27 (15-30)	28 (24-30)
MoCA	24 (13-28)	25.5 (17-29)
Verbal fluency test	9 (2-10)	9 (5-10)
Clock drawing test	12 (5-18)	11 (5-21)

*Median (min-max)

Table1.

Results: Here we examined whether polymorphic variant Val66Met are relevant to idiopathic PD in Russia. There were no differences in genotypes distribution and alleles frequencies between PD patients and controls. Furthermore, there was no difference between Met66 allele frequency in PD patients with and without cognitive impairment. Cognitive functions in BDNF 66Met allele carriers were compared to carriers of Val/Val genotype. MMSE score in Met66 carriers has no difference compare to Val/Val carriers, p=0,241. The same results were obtained using MoCa, verbal fluency test, and clock-drawing test. (Table1)

Conclusion: Our data suggest that Val66Met BDNF polymorphism is not a risk factor for PD development and does not lead to cognitive impairment in PD.

Disclosure: The study was supported by RFBR, research project №16-54-76009 (EraNetRusPlus grant ID230)

EP3144

Targeted next-generation sequencing (NGS) as a diagnostic tool in syndromic autism spectrum disorder (ASD)

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Background and aims: Autism spectrum disorder (ASD) is a neurodevelopmental disorder, which etiological background is highly heterogeneous. Two major groups can be distinguished, syndromic and non-syndromic forms.

Aim: to analyse the diagnostic effectiveness of targeted NGS in 120 ASD patients and to estimate the frequency of monogenic forms.

Methods: Altogether 120 patient were recruited by clinicians who met the DSM-5 criteria for ASD. After Fragile-X syndrome screening we performed next generation sequencing on MiSeq platform targeted on 103 known and candidate genes related to ASD (Illumina Trusight Autism Kit).

Results: After bioinformatic analysis we found in 102 patients rare variants in 66 genes. We identified in 11 monogenic ASD forms. We diagnosed patients with Fragile-X-, CHARGE-, Dravet-, ATRX-, Familial temporal lobe epilepsy syndrome and Duchenne muscular dystrophy concomitant with ASD phenotype. In further ASD cases mutations in CNTNAP2, CREBBP, SLC9A9, NLGN3, NSD1, and CHD8 supposed to be the best candidate to explain the neurodevelopmental phenotypes. In these cases segregation analysis is running now. Phenotypically 68 patients were considered as idiopathic ASD patient, and 52 had an additional feature beside autism, noted as syndromic ASD patients. In 13% of the cases no rare variant compatible to our variant inclusion criteria was found.

Conclusion: Targeted NGS sequencing is a useful tool to diagnose monogenic ASD forms. This method is highly recommended especially in ASD patients who have additional features beside ASD as well.

Disclosure: The Project is supported by the Hungarian Government and financed by the Research and Technology Innovation Fund. KTIA-AIK-12-1-2013-0017

EP3179

Brain MRI characteristics and scoring in adult onset Krabbe disease

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Background and aims: Krabbe disease is a recessively inherited lysosomal storage disease due to decreased galactocerebrosidase activity. Adult onset is rare, however probably underdiagnosed. Brain MRI showing a leukodystrophy is of great value to achieve diagnosis. We aimed at performing for the first time a systematic analysis of brain MRI features in adult onset Krabbe disease (> 10 years old).

Methods: Authors of articles describing adult onset Krabbe disease patients were asked to share the first available brain MRI of their patient. A score was established to describe the brain MRIs, with quantification according to severity (from 0 to 4 for non fascicular structures, from 0 to 2 for fascicular structures). Two neuro-radiologists first scored separately the MRIs, then reached a consensus for final scoring.

Results: 13 patients were included in the study. Pyramidal tract was the most frequent structure showing abnormal T2 hypersignal (100% of patients), however with some distinctions along the tractus : medial pre central gyrus (mean score 2.8/4), lateral pre central gyrus (1.77/4) and corona radiata (1.7/2) were highly abnormal whereas internal capsula (0.96/2), mesencephalon (0.69/2), pons (0.42/2) and spinal bulb (0/2) were quite spared. 9/13 patients (69%) had corpus callosum hypersignal especially in isthmus (mean score 0.69/2). Finally medial lemniscus was the most frequent abnormal structure found in posterior fossa (9/13 patients -69%-, mean score 0.96/2).

Conclusion: Upper pyramidal tract, corpus callosum isthmus and median lemniscus were the most frequently found structures with abnormal T2 hypersignals. This study should improve awareness of Krabbe disease in adult patients with leukodystrophy.

Disclosure: Nothing to disclose.

Neuroimaging

EP3145

The role of habenula and amygdala in Parkinson's disease patients with punding

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Background and aims: Punding is a poorly investigated impulsive-compulsive behavior (ICB) in Parkinson's disease (PD), causing severe threat to physical and psychosocial well-being. This study assessed whether a functional dysregulation of the habenula and amygdala, as modulators of the reward brain circuit, contributes to PD-punding.

Methods: Structural and resting state functional MRI were obtained from 22 PD-punding patients, 30 PD patients without any ICB (PD no-ICB) matched for disease stage and duration, motor impairment, and cognitive status, and 30 healthy controls. Resting state functional connectivity of the habenula and amygdala bilaterally was assessed using a seed-based approach. Habenula and amygdala volumes and cortical thickness measures were obtained.

Results: Compared to both controls and PD no-ICB cases, PD-punding patients showed higher functional connectivity of habenula and amygdala with thalamus and striatum bilaterally, and lower connectivity between bilateral habenula and left frontal and precentral cortices. In PD-punding relative to PD no-ICB patients, a lower functional connectivity between right amygdala and hippocampus was observed. Habenula and amygdala volumes were not different among groups. PD-punding patients showed a cortical thinning of the left superior frontal and precentral gyri and right middle temporal gyrus and isthmus cingulate compared to controls, and of the right inferior frontal gyrus compared to both controls and PD no-ICB patients.

Conclusion: A breakdown of the connectivity among the crucial nodes of the reward circuit (i.e., habenula, amygdala, basal ganglia, frontal cortex) might be a contributory factor to punding in PD. This study provides potential instruments to detect and monitor punding in PD patients.

Disclosure: Ministry of Education and Science Republic of Serbia (Grant #175090).

EP3146

Conventional MRI measurements in the differential diagnosis of Parkinson's disease and Multiple System Atrophy subtypes

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Background and aims: Multiple System Atrophy (MSA) is characterized by dysautonomia, extrapyramidal, cerebellar and pyramidal signs and is subdivided in MSA-P and MSA-C, depending on the predominant clinical features. Its' main differential diagnosis is Parkinson's disease (PD). The aim of this study was to implement MRI distance and surface measurements of brainstem structures to differentiate MSA-C, MSA-P and PD patients.

Methods: A total of 25 patients (8 MSA-C, 6 MSA-P and 11 PD) and 12 healthy controls were included. MRI measurements included simple brainstem distances. MRI planometry included midbrain, pons, corpus callosum and 4th ventricle surfaces. Relevant ratios of distances and surfaces, as well as the Magnetic Resonance Parkinsonism Index (MRPI) were calculated. Analysis of variance, Kruskal-Wallis and ROC curve analysis were used as appropriate.

Results: All measured brainstem distances, with the exception of midbrain (A-P) distance, pons surface, all relevant ratios and the MRPI were significantly lower in MSA-C patients. No MRI measurement could differentiate MSA-P from PD patients. MCP width was most potent in discriminating MSA-C patients (AUC=1.00, p<0.0001, 100% sensitivity and specificity, for a cut-off point of ≤7.6mm). Pons distance and surface, midbrain to pons distance and surface ratios as well as MRPI also provided excellent discriminative diagnostic value for MSA-C.

Conclusion: MSA-C can be differentiated from MSA-P and PD by a multitude of simple MRI distance and surface measurements. MSA-P did not differ from PD patients in any of the applied MRI measurements.

Disclosure: Nothing to disclose

EP3147

Baseline 18F Flortaucipir SUVR, but not amyloid or cognition, predicts cognitive decline over 18 months in Phase 2 trial subjects

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Background and aims: This study evaluates the relationships between Flortaucipir uptake and changes in cognition or function over time.

Methods: Flortaucipir scans (acquired 80-100 min post 370 MBq injection) were obtained in amyloid-positive healthy (n=5), MCI (N=47) or AD (N=30) subjects. VOI SUVR values were obtained from 1) a VOI determined by discriminant analysis to distinguish diagnostic groups (MUBADA) and 2) VOIs defined at baseline by the correlation between tau and domain-specific cognitive tests. Assessment included MMSE, ADAS-Cog, and the Functional Activities Questionnaire (FAQ). Correlations were used to compare baseline Flortaucipir or Florbetapir SUVR or cognitive scores to changes in cognition after 18 months.

Results: Strong correlations at baseline were seen between both Flortaucipir and Florbetapir SUVR relative to MMSE, ADAS-Cog and FAQ. Baseline Flortaucipir MUBADA SUVR was also correlated with all 18 month cognitive and functional change measurements (ADAS-Cog p=0.047, MMSE p=0.0007, FAQ p=0.0006). Amyloid SUVR was not correlated with 18 months changes in cognition or function, nor were baseline cognitive or functional measures correlated with changes with their respective measure. Heat map analysis showed that for most cognitive domains, MUBADA SUVR was at least as effective as the cognitive-correlation-derived VOIs at predicting 18 months changes.

Conclusion: Baseline tau was strongly correlated with 18 month change in MMSE, ADAS-Cog and FAQ, while baseline amyloid, cognitive and functional score were not. These data suggest that tau is relevant to the evolution of cognitive and functional decline in ways not evident for either amyloid or cognitive/functional measures themselves in MCI and AD patients.

Disclosure: This study is fully granted by Avid Radiopharmaceuticals a wholly owned subsidiary of Eli Lilly & Co.

EP3148

Changes in grey matter volume and functional connectivity in cluster headache versus migraine

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Background and aims: Recent MRI studies suggest in the brain of cluster headache (CH) and migraine (M) structural and functional abnormalities. However, no between-group comparison of MRI measures has been performed

Methods: Multimodal MRI was acquired on a 3T MR scanner in age-matched patients with CH (n=12), M without aura (n=13), both during attack-free period, and normal controls (NC, n=13). MRI processing was performed with FSL. Voxelwise analyses of variance were done with nonparametric permutation testing (p≤0.05, corrected)

Results: Compared with NC, higher grey matter volume (GMV) occurred in CH in the cerebellum and occipital fusiform gyrus and in M in the lateral occipital cortex (LOC). GMV was lower than in NC in the inferior frontal gyrus of CH and in the lingual gyrus of M. Compared with M, GMV of CH was higher in the cerebellum and lower in the frontal pole and LOC. Functional connectivity (FC) was, compared with NC, higher in CH in the default mode, working memory and executive networks (DMN, WMN, EN) and altered in DMN of M, with lateral increase and medial decrease. FC in WMN and EN of CH was also higher than M. FC between cerebellar and temporo-insular networks was higher in CH than M.

Conclusion: The brain of attack-free CH seems to be characterized, compared with M, by (i) GMV changes, with decrease in a classical pain processing region (frontal cortex) and increase in an atypical region (cerebellum) and (ii) increased FC in key cognitive networks, probably with a maladaptive role.

Disclosure: Nothing to disclose

EP3149

3T MRI neurography of nerve plexuses in transthyretin familial amyloid polyneuropathy: Initial experience

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Background and aims: Transthyretin (TTR) familial amyloid polyneuropathy (FAP) is a relentless length-dependent sensori-motor axonal polyneuropathy. Amyloid fibrils unevenly accumulate for years in the nerve roots, plexuses and trunks before the onset of neuropathic manifestations. Nerve plexuses, which were so far not accessible to imaging, can now be explored by MRI neurography.

Objectives: To evaluate high-resolution 3T MRI neurography of the lumbo-sacral plexuses in a cohort of consecutive TTR-FAP patients or asymptomatic carriers.

Methods: 13 individuals with pathogenic mutation of the TTR gene were included (10 symptomatic, 3 asymptomatic carriers). The median neuropathy impairment score (NIS) was 38.5/244 (range 4-102). MRI neurography of the lumbo-sacral nerve plexuses was performed at 3T, including high-resolution T2-weighted and diffusion-weighted MR sequences in the coronal and axial planes. The same MRI protocol was applied in 10 controls. Two blinded readers assessed nerve plexus calibre and signal. Nerve enlargement was defined as an increase in nerve caliber of at least 50%.

Results: Agreement between readers was excellent (kappa of 0.88). MRI neurography revealed abnormalities of nerve plexuses in both symptomatic patients and asymptomatic gene carriers. Proximal and focal enlargement of nerve plexus was visible in 5 of the 13 patients with FAP, punctiform T2-weighted hyperintensities in 10. Of the 3 asymptomatic gene carriers, all exhibited punctiform hyperintensities and one also showed focal enlargement of nerve plexus. None of these abnormalities were observed in controls.

Conclusion: MRI neurography can show abnormalities in both symptomatic patients and asymptomatic gene carriers, providing new insights regarding the diagnosis of TTR-FAP.

Disclosure: Nothing to disclose

EP3150

Assessing longitudinal iron deposition in deep grey matter nuclei with high-pass filtered phase MR Imaging in Parkinson's disease

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Background and aims: Iron accumulation plays an important role in neurodegeneration in Parkinson's disease. Susceptibility weighted imaging (SWI) is a high-resolution MR-based imaging technique for quantifying iron depositions in vivo. Phase images offer greater specificity in quantifying brain iron load. We hypothesised that high-pass filtered phase imaging may be a useful monitoring tool for longitudinal clinical characterization of PD, and we sought to investigate the clinical associations of iron depositions in deep grey matter nuclei.

Methods: We evaluated forty-two PD subjects and six age and gender matched healthy volunteers (HV) longitudinally with high-pass filtered phase imaging at baseline and after 18 months. Average phase shifts (radians) in the caudate nucleus, putamen, globus pallidus, substantia nigra (SN) and dentate nucleus (DN) were analysed using SPIN software. Longitudinal changes of bilateral radians (Δ radians) were calculated by subtracting baseline values from follow up values. Parametric correlations of regional Δ radians were conducted with Δ UPDRS part III, tremor and bradykinesia-rigidity sub-scores.

Results: PD patients showed significantly higher radians in the SN ($p < 0.001$) after 18 months, without significant change in controls. Δ SN radians positively correlated with Δ UPDRS-III ($p < 0.001$) and bradykinesia-rigidity subscores ($p = 0.001$). In addition Δ DN correlated with tremor subscores ($p < 0.01$).

Conclusion: Our results show that high-pass filtered phase imaging might offer an interesting monitoring tool to evaluate longitudinal progression of motor severity and clinical phenotypes in PD, and could be useful to assess the effect on these structures of iron chelation therapies.

Disclosure: This work was supported by Parkinson's UK (PaMIR), the Medical Research Council and FP7 EU consortium (TransEuro). Part of this work was supported by NIHR awards of the Biomedical Research Centre to the University of Cambridge/Addenbrooke's Hospital and to Imperial College London.

EP3151

Resting state nigral functional connectivity in Parkinson's disease: A cross-sectional study

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Background and aims: The clinical manifestation of neurodegenerative diseases is thought to result from disrupted functional brain networks. Parkinson's disease (PD) is a neurodegenerative disorder characterised by progressive dopaminergic neuronal loss of SNc with further dysfunction of striatal-thalamic-cortical loops. To investigate the pattern of network dysfunction resulting from SN neurodegeneration we subsequently performed a resting state fMRI cross-sectional study of nigral functional connectivity.

Methods: Twenty-nine early stage PD subjects during medication off state and twenty-six age and sex matched healthy controls were studied with resting state fMRI. Spontaneous low-frequency (0.08-0.1 Hz) blood oxygenation level-dependent (BOLD) signal intensity fluctuations of SN were used to identify significant temporal correlations with a priori striatal and motor cortical regions. For each individual the mean SN time series were correlated with the time series of striatal nuclei and the regions of the Human Motor Area Template (HMAT). Nigral seeds were divided into more and less affected sides according to clinical motor severity as assessed with UPDRS III.

Results: Nigral seed regions showed positive functional connectivity with thalamus, globus pallidus and putamen and was anticorrelated with sensorimotor cortex in both PD and HC groups. In contrast, additional negative connectivity was shown in premotor cortex (SMA and premotor dorsal areas) in PD group. Further decline of functional connectivity in premotor cortex were found in most affected SN when compared to the less affected.

Conclusion: Our results demonstrate the in vivo disrupted nigral functional connectivity using RS fMRI with the striato-thalamo-cortical structures in early PD patients, in keeping with dopaminergic neurodegeneration.

Disclosure: This work was supported by Parkinson's UK (Parkinson's magnetic imaging repository, PaMIR).

EP3152

Quantitative MRI texture analysis of enhancing and non-enhancing T1-hypointense lesions without application of contrast agent in multiple sclerosis

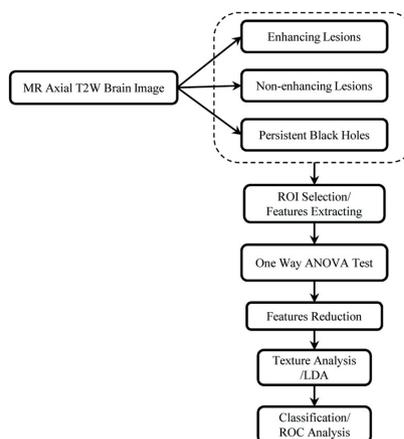
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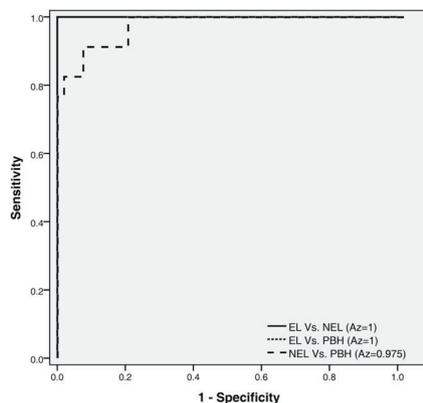
Background and aims: Gadolinium-enhanced MRI is a sensitive method to assess active inflammation in MS lesions. The aim of this study was to evaluate texture analysis (TA) in pre-contrast injection MR images to improve accuracy and to identify subtle differences between enhancing lesions (ELs), non-enhancing lesions (NELs) and persistent black holes (PBHs)

Methods: The MR image database comprised 90 patients; 30 of which had only PBHs, 25 had only ELs and 35 neither EL or PBH. These were assessed by the proposed TA method. Up to 300 statistical texture features were extracted as descriptors for each region of interest/lesion. Differences between the lesion groups were analyzed and evaluations were made for area under the receiver operating characteristic curve (Az) for each significant texture feature. Linear discriminant analysis (LDA) was employed to analyze significant features and increase power of discrimination. Lesions were classified by the 1-NN classifier.



Overview of texture analysis process in the MR brain images

Results: At least 14 texture features showed significant difference between NELs and ELs, NELs and PBHs, and ELs and PBHs. By using all significant features, LDA indicated a promising level of performance for classification of NELs and PBHs with Az value of 0.975 that corresponds to sensitivity of 94.28, specificity of 96.30%, accuracy of 95.5%. In classification of ELs and NELs (or PBH), LDA demonstrated discrimination performance with sensitivity, specificity and accuracy of 100% and Az of 1.



The diagrams of the ROC curve for texture analysis method with LDA in classification of NELs, ELs and PBHs

Conclusion: TA was a reliable method, with potential for characterization and the method can be applied by physicians to differentiate NELs, ELs and PBH in pre-contrast injection MR imaging.

Disclosure: Nothing to disclose

EP3153

Automated brain tissue and lesion segmentation in multiple sclerosis: A feasibility study in the state of Salzburg

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Background and aims: Brain atrophy and lesion load are related to clinical outcomes in multiple sclerosis (MS). Manual reading and semi-automated segmentation of magnetic resonance imaging (MRI) scans are used at institutions with scientific background. Fully-automated MRI segmentation methods could support individualized management and improve therapeutic success in clinical practice.

Aims: To assess feasibility and limitations of automated brain MRI analysis tools developed for patients with MS in a real-life setting.

Methods: We studied a cohort of 173 MS patients (64% women). Scans were acquired at ten radiology institutes in the state of Salzburg, Austria. MRI facilities were hospital based (n=5) or had private ownership (n=5). We uploaded scans for analysis of brain atrophy and total brain lesion volumes to online platforms of Icometrix/MSMetrix (Leuven, Belgium) and Jung Diagnostics (Hamburg, Germany). We further contacted the MRI providers for brain scan protocol details used for MS patients.

Results: We submitted 146 scans of 73 patients to Icometrix (25 patients with >2 scans) and 58 scans of 47 patients (7 patients with >2 scans) to Jung Diagnostics (Table 1). Reasons for rejections were lack of minimal standard requirements. These included inappropriate slice thickness, low signal to noise ratio and incomplete field of view. Detailed field strength distribution and imaging properties, see Table 2.

Table 1

	Icometrix	Jung Diagnostics
No. of submitted scans	146	58
No. of feasible scans (%)	10 (7%)	49 (85%)
Overlapping No. of identical scans	12	

MRI Scan Databases

Table 2

Institution	Field Strength (Tesla)	Slice Thickness T1 (mm)	Slice Thickness FLAIR (mm)
A	1.5	n.a.	4
B	1.5	4	4
C*	3	4	4
D*	3	0.75	4
E	1	5	3.5
F	1.5	5	5
G	3	5	2
H*	1.5	n.a.	4
I*	3	1	4
J*	1.5	1	4
Minimal standards MAGNIMS group	3	<3	<3

Legend: Overall 10 institutions (A-J, *hospital based) provided MRI scans. Field strength of the MRI scanners used in the state of Salzburg was 3 Tesla (n=4), 1.5T (n=5) and 1T (n=1). Slice thickness for FLAIR sequences were 5mm (n=1), 4 mm (n=7), 3.5 mm (n=1) and 2mm (n=1).

MRI Properties

Conclusion: Technical limitations lead to high dropout rates for scans obtained in a real-world setting. MRI protocols for FLAIR images did not comply with minimal standards proposed by the MAGNIMS group. Moreover, minimal requirements among providers of automated segmentation are not uniform.

Disclosure: Nothing to disclose

EP3154

Stroke resulting aphasia and transcranial doppler findings

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Background and aims: Out of all possible causes of aphasia stroke is the leading one (18-35%).

We examined possibility of TCD in identifying most frequently affected vessels in post-stroke aphasic patients, type of aphasia and location of brain injury.

Methods: The study included 189 patients(pts) F/M=72/117, age 59±10 years with the first acute ischemic stroke and aphasia admitted to the St Sava Hospital from January 1 to October 31, 2016.with no brain MSCT/MR findings of an earlier stroke. In the first 48 hours Color Duplex Sonography (CDS) and Transcranial Color Duplex Sonography (TCD) examinations were done .The Western Aphasia Battery (WAB) was used to provide information of the type of aphasia and MSCT/MR on location of the lesion.

Results: RESULTS: The main aphasic syndrom was Broca's aphasia (61%). In 149 pts(79%) the lesions were located at classical language centers. According to TCD and CDS 62 pts (33%) had no changes in the intracranial hemodynamics; out of 127 pts (67%) with changes, 23 pts (17%) had terminal ICA stenosis/occlusions; 56 pts (45%) hypoperfusion of the L or R MCA; 48 pts (38%) had a significant stenosis/or occlusion of the extracranial ICA, with collateral circulation (through ACoA, PCoA or OA).

Conclusion: CONCLUSION: In our study, Broca's aphasia was the most frequent aphasic syndrome in the acute stage of ischemic stroke in the territory of the MCA. The damaged lesions were in classical language functional areas. TCD is a useful noninvasive method to monitor the hemodynamic state of the circle of Willis.

Disclosure: Nothing to disclose

Neurological manifestations of systemic diseases

EP3155

Neurological involvement in Gougerot Sjogren Syndrom from central to Peripheral nervous system: Diagnosis challenge

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Background and aims: Neurological manifestations in Gougerot-Sjogren syndrome (GSS) are valued differently. This is essentially the achievement of the peripheral nervous system.

Methods: We report a series of 21 cases of neurological manifestation revealing a Sjogren Gougerot syndrome collected over a period of 12 years (2005 -2016).

Results: 95.2% of cases were female with a sex ratio of 0.05 with an average age of 42.3 years. Central involvement was noted in 9 cases with encephalic involvement in 6 cases, encephalic involvement associated with myelopathy in 2 cases. Cranial nerve involvement associated with encephalic involvement in one case. Peripheral nervous involvement was noted in 7 cases, with sensitivomotor polyneuropathy in 3 cases, the sensitive neuropathy in one case, isolated involvement of the cranial nerves in 2 cases and multiplex mononeuropathy in 1 case. Peripheral nervous involvement associated with central involvement in one case. An association with other neurological conditions in 4 cases

Conclusion: we found a concordance of the profile of the patients, with the literature, therefore the adult age and the female predominance. Central neurological involvement was predominant compared to peripheral nervous involvement, contrary to the literature. In terms of peripheral involvement, sensitivo-motor polyneuropathy was the most frequent in our series. Focal encephalic manifestations are the CNS manifestations most frequently observed in the literature, which is consistent with our study.

The neurological manifestations related to GSS are difficult to diagnose. Some neurological manifestations require systematically search for a GSS: myelopathy, neuropathy predominantly sensitive, cranial nerve damage or manifestation of MS after 50 years.

Disclosure: Nothing to disclose

EP3156

The physical anthropological factor in diagnosis of Wilson's disease

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Background and aims: Wilson's disease (WD) is a genetically based pathology and its neurological manifestations are often misdiagnosed. Thus, identification of additional diagnostic criteria is very important both for a primary and differential WD diagnosis.

Methods: An integrated anthropological examination (defining specific phenotypic variants (PhVs)) was performed in 50 patients with confirmed WD (E83.01) and 50 persons from a general population without WD and any other psychoneurological, metabolic or hepatic pathology (the control group).

Results: A positive association between presence of WD and a certain PhV was detected for Mediterranean PhV (54.00% of WD patients and 20.00% in the control; $p < 0.0005$) and for Atlanto-Baltic PhV (20.00% of WD patients and 6.00% in the control; $p < 0.05$). A negative association between presence of WD and a certain phenotypic variant (PhV) was detected for Alpine PhV (0.00% of WD patients and 32.00% in the control; $p < 0.00001$), for Paleo-European PhV (4.00% of WD patients and 22.00% in the control; $p < 0.005$), and for East-Baltic PhV (0.00% of WD patients and 8.00% in the control; $p < 0.05$).

Conclusion: The range of a grade of association between the main phenotypic variants and risk of WD was formed: positively – Mediterranean PhV (a very high grade) and Atlanto-Baltic PhV (a high grade); neutral – Dinaric PhV; negatively – East-Baltic PhV, Paleo-European PhV (a high grade), and Alpine PhV (a very high grade). These data should be taken into account in examination of patients with WD and in a differential diagnosis of doubtful cases.

Disclosure: Nothing to disclose

EP3157

Diagnostic of systemic inflammatory disorders among patients admitted for acute aseptic meningitis: An observational study

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Background and aims: The aim of this study was to identify clinical indicators for systemic inflammatory disorders (SID) in patients admitted for acute aseptic meningitis.

Methods: All consecutive adults patients hospitalized over a 4-years period for acute aseptic meningitis were included retrospectively. Exclusion criteria included inability to confirm meningitis or a diagnosis of neoplastic meningitis after chart analysis. Extra-neurological signs were recorded using a systematic panel. SID diagnosis was made according to current international criteria. A multiple logistic regression analysis was carried out to identify factors independently associated with the etiology of meningitis.

Results: 88 patients were eligible. After exclusion, 43 (46[19-82] years, 60% females) patients hospitalized for an acute aseptic meningitis were analyzed. No patient was taking drugs known to induce aseptic meningitis. Among them, 23 (53.5%) had a SID that was revealed by the meningitis in 16 (69.5%) cases. Sarcoidosis and Behcet syndrome accounted for almost half of all SID. As compared to patients with idiopathic meningitis, patients with SID displayed a higher frequency of neurological ($p=0.024$), extra-neurological signs ($p=0.007$), and abnormal cerebral MRI findings ($p=0.024$) at diagnosis. Overall, the probability of SID in patients admitted with acute aseptic meningitis was of 93.7% in patients with neurological (such as focal neurological deficits, delirium or seizure) and extra-neurological signs (such as uveitis, arthralgia, aphthous ulcers and skin lesions) but fell to 14.9% in patients with neither neurological nor extra-neurological signs.

Conclusion: Structured clinical sorting according to both neurological and extra-neurological signs help to identify patients with acute aseptic meningitis caused by a systemic inflammatory disorder.

Disclosure: Nothing to disclose

EP3158

Nonsystemic and systemic vasculitic neuropathy: Experience of 25 years in tertiary neurologic clinic

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Background and aims: Vasculitis of the peripheral nervous system (PNS) occurs rarely either in the context of systemic vasculitis or isolated (non-systemic vasculitic neuropathy-NSVN). This is the first large prospective study which aims to investigate the clinical, and pathological features of both systemic and nonsystemic vasculitic neuropathy in order to establish the clinical manifestations and to promote the earlier diagnosis of the syndrome.

Methods: Biopsies were selected from over 855 sural nerve biopsies performed at the Section of Neuropathology, Neurological Clinic of Athens University Hospital between 1985 and 2005 and were followed up until 2014. The diagnosis of vasculitis was based on established clinicopathological criteria. Complete laboratory, clinical, electrophysiological, and pathological studies were performed in all cases.

Results: Nerve biopsies of 22 (2.5%) patients were diagnosed as NSVN. Systemic vasculitis (5.8%) included: 15 rheumatoid arthritis, 9 Churg-Strauss syndrome, 7 cryoglobulinemic vasculitis, 7 Systemic lupus erythematosus, 5 Sjogren disease, 3 polyarteritis nodosa, 2 Behcet's disease, 1 Crest Ankylosing spondylitis. The pathological features were vasculitis and predominant axonal degeneration with a varying pattern of myelinated fiber loss. The vasculitic changes were found mainly in small epineural blood vessels. Mononeuritis multiplex and distal symmetrical sensorimotor neuropathy were equally frequent.

Conclusion: Although less common than systemic vasculitis NSVN should be suspected in a case of unexplained polyneuropathy without evidence of systemic involvement. Clinical and neurophysiological studies are essential for the detection of nerve involvement, but the specific diagnosis of NSVN may be missed unless a biopsy is performed.

Disclosure: Nothing to disclose

EP3159

Neurological manifestations revealing Gougerot-Sjogren syndrome: 18 cases

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Background and aims: Gougerot-Sjogren Syndrome (GSS) is an autoimmune exocrinopathy characterized by a xerophthalmia and a xerostomia. It can be primitive or secondary to another connective tissue disease. Neurological involvements are observed in approximately in 20-25% of cases, inaugural in 25% of them. Our objective is to describe the clinical, paraclinic and therapeutic aspects of 18 patients with neurological signs revealing GSS.

Methods: We studied retrospectively over a period of eleven years from 2002 to 2013, 18 patients presenting a primitive GSS revealed par neurological symptoms. Diagnosis of primitive GSS is made according to the Criteria of American-European consensus 2002. All our patients has benefited of complete assessment to confirm the diagnosis : Schirmer test, an accessory salivary glands biopsy and an immunological assessment.

Results: Eighteen patients were studied. The average of age was 44 years and the sex ratio was 0.2. Peripheral nervous system involvement was noted in 50% cases (9/18): 5 cases had sensitive-motor polyneuropathy, 3 others had cranial nerves involvement and one case had anterior horn syndrome. Central nervous system involvement was noted in 88.88% (16 cases). Multifocal signs affecting brain and spinal cord are described in 11 cases, chronic myelopathy and acute transverse myelitis in 3 cases. All patients received an oral corticosteroids, followed by a progressive regression.

Conclusion: Neurological involvements can be the first manifestation of GSS in 25% of the cases. Peripheral nervous system manifestations are well documented dominated par axonal polyneuropathy. Central nervous system involvements are under-diagnosed. Treatment of GSS neurological manifestations is not codified.

Disclosure: Nothing to disclose

EP3160

Cerebrospinal fluid findings in NeuroBehçet disease

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Background and aims: Neurological manifestations during Behcet's disease are present in 20 to 30% of the cases. Given the difficulty of differential diagnosis, the CSF study is systematic.

Objective: To study the cyto-chemical and immunoelectrophoretic profile of the cerebrospinal fluid of a series of patients monitored for NB disease.

Methods: A retrospective study over a period of 15 years (2002-2016) of patient's files admitted for NB diseases (international criteria for NB disease). Cerebral imaging and CSF study were performed for all our patients

Results: 38 NB disease cases were recruited. The neurological form was inaugural in 68.4%. The appearance of CSF was clear in 34 patients, disturbed in 3 and hematic in only one case. There was hyperproteinorachy in 16 patients (42.1% average rate of 0.85 g/l). Glycorrachia was normal in all our patients (0.58g / l). Lymphocytic meningitis was found in 17 cases (44.7%). CSF isofoculation was performed in 16 patients (65.5%). The IgG index was increased in 4 patients (10.5%). In immunoelectrophoresis, oligo clonal bands were found in two patients (5.2%).

Conclusion: The presence of predominantly lymphocytic meningitis is classic in NB. Where as, an intrathecal synthesis of IgG and oligoclonal bands exclusively in CSF are less described. Our results indicate a B and T cell involvement in NB. Indeed, the activation of autoreactive T cells with involvement of cytokines and pro-inflammatory transcription factors would be proved.

Disclosure: Nothing to disclose

EP3161

Early diagnosis of diabetic neuropathy in young patients with type 1 DM – a 10-yr follow-up studyG. Hajas¹, V. Kissova², M. Brozman¹¹*Department of Neurology, Teaching hospital Nitra, Nitra, Slovakia*, ²*Department of Internal Medicine, Teaching hospital Nitra, Nitra, Slovakia*

Background and aims: The main objective of this work was to follow-up the development of peripheral neuropathy and its severity in patients with type 1 diabetes over 10 years. We observed potential risk factors and their impact on the development of neuropathy. The other objective was longitudinal study of electrophysiological parameters.

Methods: The prospective study included 62 patients with type 1 diabetes aged 13.9±5.9 yr, with diabetes duration of 5.6±5.1 yr, treated with an intensified insulin regimen. All patients underwent a neurological examination, nerve conduction study (NCS) and biothesiometry three times (baseline, after 5 yr, after 10 yr).

Results: During the follow-up there was an increase in DN prevalence from 24.2% to 62.9% ($p<0.001$). The proportion of patients with subclinical neuropathy increased from 17.7% to 46.8% ($p<0.001$), patients with clinical neuropathy from 6.5% to 16.1% ($p<0.001$). The main contribution factors for rapid growth of the DN prevalence were poor glycaemic control, diabetes duration and patient's age. Regarding the conduction parameters, the most significant changes were observed in sural SNAP amplitude (5.2 m/s, $p<0.001$) and sural NCV (8.2 uV, $p<0.001$).

Conclusion: The results of the study demonstrated a progressive increase in the DN prevalence over time, in particular its subclinical stages. The long-term poor glycaemic control was a determining factor in the rapid DN development. The sensory conduction parameters deteriorated faster than the motor parameters. The study is one of few of those in type 1 DM, which in relation to risk factors assess not only the presence of neuropathy, but also its severity.

Disclosure: Nothing to disclose

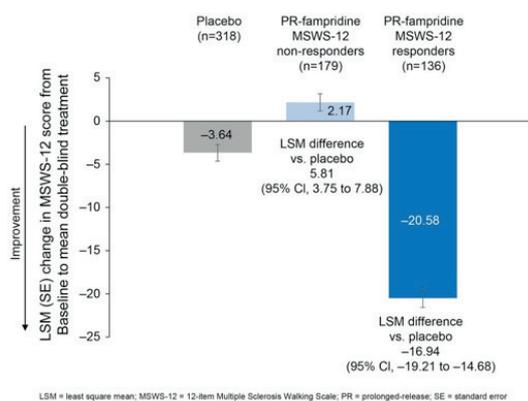
EP3162

Prolonged-release fampridine demonstrates rapid and sustained clinically meaningful improvements in walking ability over 24 weeks: MSWS-12 responders in the ENHANCE studyJ. Hobart¹, T. Ziemssen², P. Feys³, M. Linnebank⁴, A. Goodman⁵, R. Farrell⁶, R. Hupperts⁷, V. Englishby⁸, M. McNeill⁸, I. Chang⁹, G. Lima⁹¹*Plymouth University Peninsula Schools of Medicine and Dentistry, Plymouth Hospitals NHS Trust, Plymouth, United Kingdom*, ²*University Clinic Dresden, Dresden, Germany*, ³*BIOMED-REVAL, Hasselt University, Diepenbeek, Belgium*, ⁴*University Hospital Witten Herdecke, Witten, Germany*, ⁵*University of Rochester School of Medicine and Dentistry, Rochester, NY, USA*, ⁶*National Hospital for Neurology and Neurosurgery, University College London Hospitals, London, United Kingdom*, ⁷*Zuyderland Medisch Centrum Sittard, Maastricht University, Maastricht, Netherlands*, ⁸*Biogen, Maidenhead, United Kingdom*, ⁹*Biogen, Cambridge, MA, USA*

Background and aims: The international Phase 3, double-blind, placebo-controlled ENHANCE study (NCT02219932) was the largest and longest randomised trial of prolonged-release (PR) fampridine. ENHANCE demonstrated that significantly more subjects had clinically meaningful improvements in walking ability, as assessed by the self-reported Multiple Sclerosis Walking Scale-12 (MSWS-12), with PR-fampridine versus placebo (43% vs. 34%; odds ratio=1.61; $p=.006$) over 24 weeks. This analysis evaluated the magnitude of mean change in MSWS-12 score over 24 weeks, based on clinically meaningful subject-level improvement.

Methods: An MSWS-12 responder was prospectively defined as an ≥ 8 -point mean reduction (improvement) in MSWS-12 score over 24 weeks; least-square-mean (LSM) analyses used a mixed effects model for repeated measures, adjusted for screening EDSS, baseline MSWS-12, baseline TUG speed, age, and prior aminopyridine as covariates (missing data handled using multiple imputation).

Results: PR-fampridine-treated MSWS-12 responders demonstrated an LSM improvement of -20.58 points from baseline over 24 weeks; a small mean improvement was observed in the placebo group (-3.64 points), while MSWS-12 non-responders worsened slightly (+2.17 points; see figure). In PR-fampridine-treated MSWS-12 responders, improvements were detected as early as Week 2 and were sustained throughout the treatment period.



Least square mean change (LSM) in MSWS-12 score from baseline over 24 weeks in the placebo group and PR-fampridine-treated MSWS-12 responder and non-responder subjects. LSM, LSM difference, standard error (SE) calculated using mixed effects model for repeated measures.

Conclusion: Over 24 weeks, PR-fampridine-treated MSWS-12 responders experienced clinically meaningful improvement from baseline—a notable finding given the skewed nature of baseline scores across groups. Whilst the mode of action of PR-fampridine is understood, the pathophysiological explanation of MSWS-12 responders remains unclear. Therefore, MSWS-12 responders cannot be predicted a priori. Nevertheless, the fast-acting nature of PR-fampridine enables quick and efficient identification of MSWS-12 responders in clinical practice.

Disclosure: This study was funded by Biogen; medical writing support for the development of this abstract was provided by Excel Scientific Solutions and was funded by Biogen.

EP3163

Fabry disease: What should we know about neurologic involvement and MRI findings?

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Background and aims: Fabry disease (FD) is an X-linked inborn error of glycosphingolipid catabolism, caused by abnormalities in GLA gene leading to deficiency in α -galactosidase A and pathological accumulation of predominantly globotriaosylceramide into vascular endothelial, neural, renal cells, and cardiomyocytes. FD may lead to life-threatening complications such as kidney damage, heart attack and stroke. Imaging, clinical manifestations, lab data set and genetic testing play an important role in sustaining an early diagnosis of FD.

Methods: To present and illustrate the neurological manifestations and brain MRI findings of FD.

Material and Methods: 8 patients aged 20 to 59 years old, were tested for enzyme activity and gene mutations and were examined for cardiac, renal, dermatological and neurological involvement, including brain MRI and nerve conduction studies.

Results: All patients had chronic kidney disease, hypohidrosis and acroparesthesia; 4 patients had a previous ischemic stroke; 2 patients presented hearing loss; 6 patients presented angiokeratomas, and one patient presented cornea verticillata. Cardiac involvement was found in 5 patients. Brain MRI showed ischemic stroke or white matter hyperintensities by involvement of small-vessels. Nerve conduction studies showed no pathological changes. Six patients received enzyme replacement therapy.

Conclusion: Cerebral microangiopathy, ischemic stroke, autonomic dysfunction manifested as hypohidrosis and small fiber neuropathy were the neurological findings in our patients with Fabry's disease. MRI represents the most sensitive method to detect CNS involvement in Fabry disease and to monitor CNS lesions under enzyme replacement therapy. A multidisciplinary team is essential to establish an early diagnostic of FD.

Disclosure: Nothing to disclose

EP3164

Neurological and clinical findings in patients with tuberous sclerosis before and after treatment with Everolimus

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Background and aims: Tuberous sclerosis complex (TSC) is an autosomal-dominant, neurocutaneous, multisystem disorder caused in 1/3 of cases by mutations in two tumor suppressor genes, TSC1 and TSC2. The classic clinical triad include in TSC facial angiofibromas, seizures, and mental retardation. Imaging plays an important role to assess TSC lesions and the evolution under treatment. Everolimus is an mTOR inhibitor used in a number of clinical indications including TSC.

Methods: To present and illustrate classical imaging findings of TSC. To investigate the efficiency and safety profile of Everolimus treatment in patients with TSC.

Methods: Eight patients aged 25 to 50 years old, half of them with epileptic seizures were diagnosed with TSC and treated with Everolimus for 7 to 15 months. Neurological examination, brain magnetic resonance imaging (MRI), electroencephalography (EEG), thoracic and abdominal computed tomography (CT), cardiologic, dermatological and ocular examination were performed before and after Everolimus treatment. Serum levels of Everolimus were also monitored.

Results: All patients presented typical brain MRI lesions (cortical and subcortical tubers, subependymal nodules and radial migration lines), renal angiomyolipomas and cutaneous angiofibromas. Pulmonary lesions were found in 3 cases. Everolimus treatment induced a decrease of brain tubers and epileptic seizures in 10 patients and a reduction of renal angiomyolipomas, cutaneous angiofibromas and pulmonary lesions in all patients. Stomatitis was the main adverse event that was reported.

Conclusion: Everolimus treatment reduced the brain, kidney, cutaneous and pulmonary lesions in TSC patients and was well tolerated. Epileptic seizures were diminished in the majority of patients.

Disclosure: Nothing to disclose

EP3165

Cognitive complaints in patients with active Systemic Lupus Erythematosus and past neuropsychiatric symptoms

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Background and aims: Cognitive complaints are common in patients with systemic lupus erythematosus (SLE). Their association with disease and non-disease related factors have been inconsistently reported. We studied their relation to disease related factors including disease activity, neuropsychiatric history and non-disease related factors such as anxiety or depression.

Methods: We used cognitive symptoms inventory (CSI) for measuring cognitive impairment at 3 time-points 12 months apart/2015-2016/ and Hospital Anxiety and Depression Scale (HADS)-HADS- A and D. Disease activity was measured by SLEDAI.

Results: 93 SLE patients were recruited at baseline (T0). Among them 59 had first re-evaluation (T1) and 34 had second re-evaluation (T2) at 12-month interval. Majority (72%, 24/34) of patients had stable CSI whereas 5.5% (2/34) of patients worsened CSI over 12 months. At T0, multivariate analysis revealed that higher CSI was associated with history of NPSLE ($p=0.005$) and psychiatric disease ($p=0.04$), higher HADS-A ($p<0.001$) and HADS-D ($p<0.001$) scores. CSI of active patients ($SLEDAI>6$) was not different from inactive patients. It did not change despite regression of disease activity in 12 months. There was no difference in CSI between T0 and T1 regardless of history of NPSLE, change in anxiety and depression at T1 ($HADS-D>11$ as cutoff). Multivariate linear regression analysis revealed change in HADS-A as the only significant predictive factor of change in CSI over time ($\beta=0.774$, 95% CI 0.43 – 1.12, $p<0.001$).

Conclusion: 11.5% of SLE patients reported persistent cognitive symptoms. CSI had worsened in patients with NPSLE and psychiatric illness, anxiety or depression.

Disclosure: Nothing to disclose

EP3166

Neuropathic pain in systemic disease: Clinical and electrophysiological features and therapeutic approach

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Background and aims: Pain is a common symptom in patients with systemic diseases. In addition to joint and muscle pain, neuropathic pain can worsen their quality of life.

We describe herein the clinical and electrophysiological feature of patients with systemic diseases and presenting for neuropathic pain and its effect on the quality of life.

Methods: Patients with various systemic diseases and referred to our department for neuropathic pain assessment from January 2016 to December 2016 were included. All patients had neurological examination, electromyography with nerve conduction study (NCS) and evaluation with the neuropathic pain questionnaire (NPQ) and quality of life assessment (McGILL QoL questionnaire). Response to medication was also related.

Results: Thirty-three patients were included (sex ratio= 0.36; mean age= 41.8 years). Underlying systemic disease was systemic lupus (16 patients, 48%) primary Sjögren syndrome (10 patients, 30%) scleroderma (4 patients, 12%) and sarcoidosis (3 patients, 9%). Mean NPQ score was 7.2 (5-10) and mean McGILL QoL questionnaire was 54 (33-76). NCS revealed axonal sensory or sensory motor neuropathy (30%), mononeuropathy multiplex (24%) and radiculopathy (9%). NCS did not show any abnormality in 12 patients (36%) suggesting small fiber neuropathy. Poorer quality of life was associated with mononeuropathy multiplex ($p<0.01$) and systemic lupus ($p<0.05$). Treatment options included tricyclic antidepressants, pregabalin and carbamazepin. Monotherapy was insufficient in 75% of patients and 36% of them were not satisfied despite the association of two or more molecules.

Conclusion: Neuropathic pain can represent an irritating thorn in the course of various systemic diseases. Adequate treatment can be challenging in order to improve patients' quality of life.

Disclosure: Nothing to disclose

EP3167

The assessment of brain metastases risk in cancer patients: The influence of primary tumor location, histological and immunohistochemical aspects (a retrospective observational descriptive study)

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Background and aims: The aim of this study was to identify cancer patients with high risk of brain metastases, in this way improving early detection of cases.

Methods: Retrospective observational descriptive study on 396 cancer patients admitted in hospital between 2013 and 2016, which received clinical neurological exam and brain CT/MRI in selected cases. Data regarding primary cancer location (breast, upper/lower digestive, small and non-small lung cancer-SCLC, NSCLC-,urogenital, skin, head and neck, others), histological and immunohistochemical characteristics were collected from the medical records. Statistical analysis was performed using SPSS Statistics v.23.0 (statistical significance assumed at $p<0.05$).

Results: Mean age (\pm SD) was 61.62 ± 11.31 years. 94 patients had brain metastases (23.7%). Brain metastases were significantly correlated with younger age ($p=0.001$) and lung cancer ($p=0.002$). Upper and lower digestive cancers ($p=0.016$ and $p=0.034$) and head and neck cancers ($p<0.001$) correlated negatively with brain metastases. Patients with SCLC had more brain metastases than patients with NSCLC (46.6% versus 36.20%, without statistical significance, $p=0.555$). Negative hormone receptor status breast cancer patients had more frequently brain metastases than positive ones (40.90% versus 21.05%; $p=0.093$) and those with more than 70% of tumoral cells having hormone receptors seemed protected from brain metastases ($p=0.013$).

Conclusion: This work allowed identification of cancer patients with higher and lower risk for brain metastases. This is an important step in developing better future screening and early detection strategies thus facilitating early treatment and survival improvement

Disclosure: Nothing to disclose

Neuro-oncology

EP3168

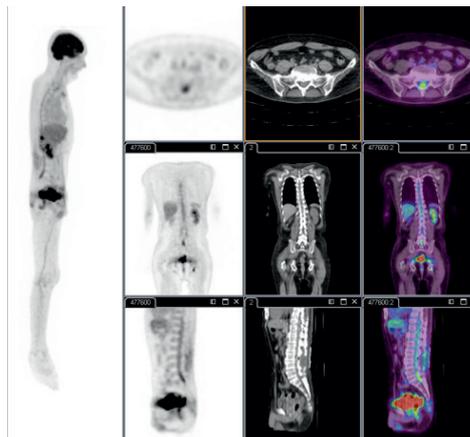
Primary Leptomeningeal Lymphoma presenting as low back pain and dementia: A case report

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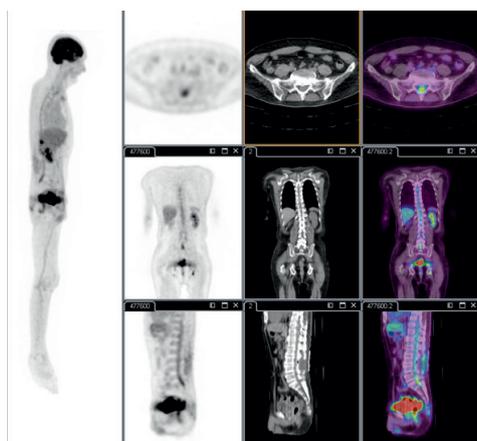
Background and aims: Primary leptomeningeal lymphoma (PLL), also called primary meningeal or dural lymphoma, is an extremely rare condition, with only a handful of cases reported in literature. Most often, these are misdiagnosed as other disease entities more commonly observed in practice. It is important to develop suspicion for leptomeningeal malignancy in atypical cases, especially those unresponsive to treatment, as the overall median survival for PLL is only 24 months. Currently, there are no clinical algorithms that may guide clinicians to clinching a diagnosis of a primary leptomeningeal lymphoma.

Methods: This paper discusses a case of leptomeningeal lymphoma that initially presented as low back pain and dementia. He was initially treated for tuberculous meningitis. However, after numerous imaging studies which showed dural enhancement from the cervical to lumbosacral spine, most markedly in the cauda equina, a malignant process was suspected. A dural biopsy with immunohistochemistry confirmed the diagnosis of leptomeningeal lymphoma. A primary malignancy was ruled in after PET CT showed no other sites of high metabolic activity. His dementia is attributable to the communicating hydrocephalus appreciated in his cranial imaging studies.



Conclusion: Primary Leptomeningeal Lymphoma is a rare disease that presents with a wide array of non-specific symptoms and is often misdiagnosed. A good index of suspicion is needed in patients who show atypical symptoms incompatible with other disease processes.

Disclosure: Nothing to disclose



Results: A ventriculo-peritoneal shunt was inserted and he underwent six cycles of Methotrexate with Rituximab infusions. The patient is alive and well with almost a normal neurological status except for residual dementia symptoms

EP3169

Cancelled

EP3170

Paraneoplastic neurological syndromes in Algeria: Clinical heterogeneity and atypical revelation patterns

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Background: Paraneoplastic neurological syndromes (PNSs) are rare autoimmune disorders that occur in association with cancer and are not explained by a metabolic, metatarsal, infectious or iatrogenic complication.

Aims: To study the clinical and paraclinical profiles of NPS in a hospital series.

Describe the peculiarities of these PNSs and compare them with the data of the literature.

Methods: A monocentric, retrospective study of PNSs supported in the Neurology department of Ait Idir Hospital in collaboration with the Immunology of the Pasteur Institute of Algeria.

Results: We included 12 patients, 10 men and 2 women, with SNPs with anti-neural antibodies positive. Antibodies found were anti-Yo (n=4), anti-Ma 2(N=2), anti-amphiphysin (n=1), anti-Zic (n=1) and anti-NMDAR (n=1). Two other patients had a POEMS. Most patients had a combination of at least two antibodies.

Conclusion: The SNPs described in our patients were characterized by high heterogeneity clinical and atypical modes of revelation. A postinfectious presentation subacute was particularly noted. PNSs can be revealed in atypical and deceptive presentations. Their recognition is, however, crucial for early care and better prognosis

Disclosure: Nothing to disclose

EP3171

Anti-Ri-antibody paraneoplastic syndrome with complete horizontal ophthalmoplegia

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Background and aims: Paraneoplastic neurological disorders associated with anti-Ri-antibodies mostly present with opsoclonus-myoclonus-ataxia. Anti-Ri-antibodies have been mainly reported in patients with breast cancer although gynecological tumors and small-cell lung cancer (SCLC) are identified, too. Ophthalmoplegia without opsoclonus is very rare. We present a woman with SCLC who had atypical anti-Ri-antibody paraneoplastic syndrome presenting as complete horizontal ophthalmoplegia and truncal ataxia.

Methods: A 59-year-old woman with subacute onset of bilateral horizontal gaze palsy and gait disturbance. She has a history of hypertension, diabetes and smoking. Neurologic examination revealed complete horizontal gaze palsy without opsoclonus-myoclonus. Diplopia wasn't reported. She presented a wide-based gait and couldn't perform tandem-gait.

Results: Her CSF showed high cell count, normal protein values, and negative cytology and viral markers. Serum's immunofluorescence analysis revealed anti-Ri-antibodies. Body-CT showed a solid lesion in left lower lung lobe with pathological lymph nodes and bilateral adrenal nodules. Fine-Needle-Aspiration through bronchoscope revealed a cytology compatible with SCLC. Brain-MRI revealed a high-signal-intensity lesion in the pontine tegmentum that wasn't enhanced with gadolinium. She was diagnosed with anti-Ri positive paraneoplastic Rombencephalitis, secondary to SCLC. She was treated with high-dose intravenous methylprednisolone pulse therapy, 1gr for 5 days without response and started standar chemotherapy (Carboplatin plus etoposide). Neurological deficits persisted during the subsequent chemotherapy.

Conclusion: Anti-Ri-antibody-associated paraneoplastic syndrome has been linked to ataxia and opsoclonus-myoclonus. However, even in the absence of opsoclonus, oculomotor dysfunction is usually prominent and the brainstem is a major site of autoimmunity. This case, showing an Anti-Ri-antibody-associated syndrome with oftalmoplegia without opsoclonus, supports the clinical disparity of this entity.

Disclosure: Nothing to disclose

EP3172

Aggressive paraneoplastic encephalo-myelo-polyradiculoneuritis with anti-VGCC antibodies and anaplastic lymphoma in a 17-year-old patient: A case report

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Background and aims: Paraneoplastic neurological syndromes (PNS) in lymphomas have important differences compared with those in solid tumors. Classical PNS are rarer; onconeural antibodies are absent in most PNS; and at the time of diagnosis, lymphomas in people with PNS are already extended. This makes the diagnostic of PNS in lymphomas challenging

Methods: We report the case of a 17-year-old girl with an aggressive form of encephalo-myelo-polyradiculoneuritis associated with anti-VGCC antibodies which led to the discovery of anaplastic lymphoma

Results: The patient presented with subacute headache, vomiting and drowsiness, cerebellar ataxia and axonal sensory-motor polyradiculoneuritis. These were followed by opsoclonus, urinary retention, severe limb weakness and dysarthria. The clinical peak was reached at 3 weeks from onset. Extensive workup ruled out infection. Brain MRI showed mild hyperintensity in the pons and cerebellar peduncles. Immunophenotyping from CSF was normal. Extensive screening of antineuronal antibodies was negative except for VGCC N and P/Q antibodies. The pathology from an axillary lymphadenopathy showed a CD30+, ALK-anaplastic lymphoma. Despite repeated courses of ivIg, plasma exchange, aggressive immunosuppression and cytostatic chemotherapy she relentlessly worsened requiring nasogastric feeding and mechanical ventilation, and died at 2.5 months from onset.

Conclusion: Apart from cerebellar degeneration in Hodgkin's lymphoma and poly/dermatomyositis in both Hodgkin's and non-Hodgkin's lymphoma, other PNS are very rare in people with lymphoma. Of our knowledge, this is the first reported case of encephalo-myelo-polyradiculoneuritis with anti-VGCC antibodies associated with anaplastic lymphoma. Screening for neoplasia in progressive subacute unexplained neurological syndromes is of utmost importance

Disclosure: Nothing to disclose

EP3173

Presenting features, referral pathways, and waiting times for patients with glioblastoma multiforme: A retrospective cross-sectional analysis

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Background and aims: Glioblastoma multiforme (GBM) is a highly malignant form of glioma with a universally poor prognosis, despite advances in treatment and the introduction of national UK cancer waiting time targets. We aimed to assess the common presenting features, and the effects of referral pathway on patient outcomes.

Methods: We collected data for all cases diagnosed locally between 2009 and 2016, including clinical features, referral route, and mortality. Patterns of presenting signs and symptoms were compared with previous studies, and current NICE guidelines for the referral of suspected brain cancer. Timelines for discussion, investigation and treatment were constructed for each patient, and compared for evidence of variation in care and clinical outcomes based on referral route.

Results: Of 58 cases, emergency admissions accounted for 69%, followed by non-urgent GP referrals (19%) and urgent referrals (9%). Presenting features were highly variable and included headache, weakness, seizures, and cognitive deficits. There was no difference in waiting time to first specialist discussion, biopsy, or treatment between emergency and urgent referral cases. Non-urgent referrals experienced longer waits for specialist discussion ($p=0.037$) and biopsy ($p<0.001$). However, this had no impact on time to initiation of treatment or on 1, 3, or 5-year survival.

Conclusion: Our study shows that the majority of patients with high-grade gliomas are not detected via the urgent referral system, and that referral route has a negligible impact on patient care. This highlights significant human and financial resources that could be more productively deployed elsewhere, and the need for more effective strategies of referral and investigation.

Disclosure: Nothing to disclose

EP3174

Oligodendroglioma with a microscopic pleomorphic xanthoastrocytoma-like perivascular lesion

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Background and aims: The coexistence of diffuse and localized glioma has rarely been reported. Herein, we present a histological and genetic case study of concurrent oligodendroglioma and pleomorphic xanthoastrocytoma (PXA).

Methods: A 48-year-old male presented with a generalized seizure. Magnetic resonance imaging (MRI) revealed a non-enhanced mass in the left frontal lobe, which was suggestive of low-grade glioma. The patient was monitored with serial MRI, which revealed slight enlargement of the tumor. The patient underwent a craniotomy and tumor resection about 18 months after the initial symptoms appeared.

Results: Examination of the surgical specimen showed an oligodendroglioma containing a localized astrocytoma element, which corresponded to PXA, measured only 0.9 mm in greatest diameter, and was almost completely limited to the Virchow-Robin space of the superficial cortex. No elevated mitotic activity, microvascular proliferation, or necrosis was found in either tumor. Immunohistochemistry confirmed that each tumor was mIDH1R132H-positive, p53-negative, and ATRX-positive. Genetic analysis demonstrated that each component harbored an IDH1 G395A mutation, 1p/19q co-deletion, and a TERT promoter C228T mutation, whereas no TP53 or BRAF mutations were detected. The diffuse glioma met the diagnostic criteria for oligodendroglioma, IDH-mutant and 1p/19q-codeleted, according to the 2016 World Health Organization classification of tumors of the central nervous system. Genetic testing of the microscopic PXA-like lesion was performed with laser microdissection.

Conclusion: Genetic analysis confirmed that this case involved an unusual type of combined glioma of the same genotype rather than a collision tumor. This case provides further insights into the pathogenesis of glioma.

Disclosure: Nothing to disclose

EP3175

Diagnostic markers of paraneoplastic peripheral neuropathy in patients with breast cancer

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Background and aims: Paraneoplastic peripheral neuropathy (PPN) occurs in 3-20% of patients with breast cancer (BC). Onconeural antibodies appear in the blood of patients and lead to the appearance of neurological symptoms in 1-4 years before the diagnosis of cancer.

Objective: To detect the clinical, neurophysiological and neuroimmunological markers PPN in patients with BC.

Methods: 61 women with BC and complaints of weakness and sensory disorders in the limbs (mean age: 53.1±9.5 years; BC mean duration: 2.5±1.3 years; BC stages I-IV). Detection onconeural of antibodies in the serum of patients were carried out using Neuronal Antigen Profile EUROLINE (IgG) in vitro by immunoblotting. Bioelectric potentials of peripheral nerves of the limbs were recorded using stimulation electroneuromyography.

Results: Clinical symptoms symmetric distal polyneuropathy detected in 93% of patients. Movement disorders dominated -53%. Sensory motor polyneuropathy occurs in 47% of patients. Neurological symptoms PPN occurred an average for 2 years in 67% of women (24,0 (8,0-30,0) months) to the diagnosis of BC. Results of electromyography (low amplitude of motor response and speed of the nerves) are correlated with the clinical picture in 54% of patients. Onconeural antibodies found in the sera of 71% of patients (anti-CV2-18%; anti-Hu-7%; anti-Ma2-58%; anti-Yo-17%).

Conclusion: Disorders of the peripheral nervous system in BC is associated at the first place with autoimmune response to antigens produced by tumor cells. Clinical manifestation of PPN ahead of clinical manifestation of cancer. Onconeural antibodies in the serum of patients with neurological symptoms polyneuropathy can be used for BC in the early stages.

Disclosure: Nothing to disclose

EP3176

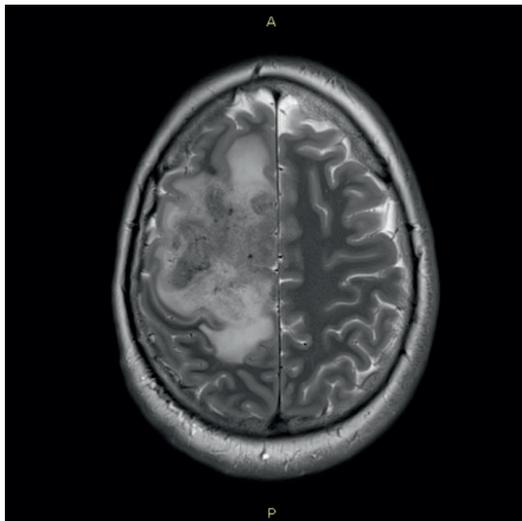
Paraneoplastic cerebral cytotoxic lymphocytic vasculitis associated with anaplastic ganglioglioma – a case report

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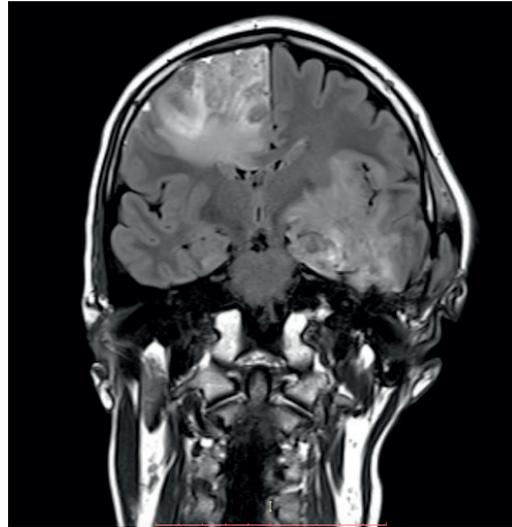
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Background and aims: Gangliogliomas are rare (1.3% of all primary brain tumours) and consist of both neuronal and glial elements. Anaplastic gangliogliomas are even rarer, accounting for 1-5% of all gangliogliomas. Paraneoplastic T-cell vasculitis of the CNS is very rare.

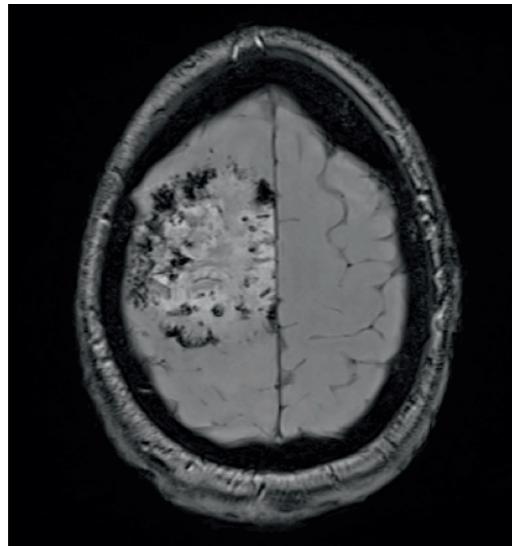
Methods: We report the case of a 25-year-old man with a 6-month history of episodic anxiety, followed by left hemiparesis and partial complex seizures. A brain MRI revealed two large enhancing tumours (left temporal and right fronto-parietal) with necrotic areas and important oedema. The tumour in the temporal lobe was resected. The pathological examination showed a massive lymphocytic vascular and perivascular proliferation with activated CD8+CD4- T-cells and no lymphomatous cells. Infections that could mount the T-cell response (HIV, HTLV1 and Toxoplasma gondii) were ruled out. Hybridization in situ for EBV was negative. Further tissue immunocytochemistry showed anaplastic ganglioglioma (WHO 9505/3).



Axial T2-weighted MR image showing the fronto-parietal lesion



Coronal fluid attenuation inversion recovery brain MR image showing bilateral lesions suggestive of vasculitis



Susceptibility weighted MR image showing multiple bleedings in the periphery of the fronto-parietal lesion

Results: The massive vasogenic oedema secondary to the vasculitic cytotoxic T-cell response led to a relentless clinical worsening despite strong and early immunosuppression with high dose steroids, cyclophosphamide, methotrexate and ivIg, and a left decompressive hemicraniotomy. After four weeks the patient died.

Conclusion: The massive cytotoxic lymphocytic vasculitis in the presence of an aggressive type of brain tumour suggests a paraneoplastic mechanism. This is the first case reported of a secondary T cell response directed against brain vessels probably driven by anaplastic ganglioglioma.

Disclosure: Nothing to disclose

EP3177

Bilateral vestibulocochlear nerve enhancement as an isolated brain MRI sign of leptomeningeal carcinomatosis

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Background and aims: Leptomeningeal carcinomatosis occurs in approximately 5% of patients with cancer. Clinical manifestations can be highly variable and may affect both central and peripheral nervous system. Involvement of multiple cranial nerves is common, with III, IV, VI and VII nerves most often affected. Isolated vestibulocochlear nerve involvement is rare. This report describes a case of a patient with vertigo and a bilateral VIII nerves enhancement as clinical-imagological presentation of leptomeningeal carcinomatosis.

Results: A 56-year-old woman presented, at our emergency room, with a one week history of vertigo and imbalance. She was a smoker and had a history of lung adenocarcinoma diagnosed one year before, treated with pulmonary lobectomy and chemotherapy. She denied other symptoms, namely headache. On examination, she had a right gaze-evoked nystagmus and a sensory ataxia with positive Romberg's sign. She had no meningism and no obvious other neurological signs and the fundus oculi examination was normal. Head computed tomography (CT) showed no abnormalities. Brain MRI showed a contrast enhancement of both vestibulocochlear nerves. CSF analysis showed pleocytosis and the cytology revealed malignant cells, compatible with a diagnosis of metastatic adenocarcinoma.

Conclusion: Our data show that vestibulocochlear symptoms represent the only clinical manifestation in a small proportion of patients (about 10%) with leptomeningeal carcinomatosis. Isolated bilateral vestibulocochlear nerve enhancement is a rare imagological finding and should be considered in the differential diagnosis even in the absence of associated clinical symptoms and neuroimaging alterations more suggestive of meningeal carcinomatosis.

Disclosure: Nothing to disclose

EP3178

Glioblastoma as differential diagnosis of autoimmune encephalitisA. Vogrig¹, B. Joubert², F. Ducray², L. Thomas², K. Decaestecker³, S. Grand⁴, J. Honnorat²

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Background and aims: The diagnosis of autoimmune encephalitis (AE) relies on clinical, MRI and laboratory criteria. Since autoantibody (Ab) testing is not available in many centers, and its negativity does not always exclude the diagnosis, Ab-status was not included in the recent consensus criteria. By using these criteria, it is possible that other conditions (AE-mimics) could be diagnosed as AE. This study examined glioblastoma patients that present initially as AE.

Methods: Retrospective case series of patients referred for suspected AE (possible, probable or definite, using the 2016 criteria), that later received a final diagnosis of glioblastoma according to 2016 WHO criteria. An extensive literature search was also conducted for similar existing cases.

Results: 10 patients were included for analysis (4 from our series and 6 from the literature). 60% were male; median age was 63. Initially, a diagnosis of AE was clinically suspected based on: working memory deficits (80%), psychiatric symptoms (60%), seizures (50%) (including status epilepticus in 30%). Initial Brain MRI was not in favor of a typical glioblastoma pattern and showed unilateral (50%) or bilateral selective limbic involvement. Three patients exhibited initial slight contrast enhancement. When MR-spectroscopy was performed (3 cases), an increased Cho/NAA ratio was detected. A clear inflammatory CSF was present in 4 patients and 2 showed Ab-positivity (NMDAR, VGKC). Median delay between suspicion of AE to GBM diagnosis was 3 months.

Conclusion: An alternative diagnosis of glioblastoma should be considered in patients presenting initially as AE, especially if they are middle-aged/elderly, male, and with an atypical MR-spectroscopy.

Disclosure: Dr Vogrig reported receiving a fellowship grant from the European Academy of Neurology (EAN).

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