

Posterior Reversible Encephalopathy Syndrome as the initial clinical manifestation of Neuro-Behcet's Disease: A case report./h3

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Neuro-Behcet (NBD) is a presentation of Behcet's Disease where the central nervous system (CNS) is affected; this insult is too, heterogeneous in its features. Specifically, NBD largely consists of two clinical entities affecting the CNS: the more common form of meningoencephalitis arising from parenchymal insult, and a phenotype consisting of cerebral sinus thromboses' sequelae (non-parenchymal NBD). Among variations reported in the literature, reversible posterior cerebral venulitis has been previously reported as a potential phenotype of the non-parenchymal NBD variant. In a similar manner, Posterior Reversible Encephalopathy Syndrome (PRES) is a heterogeneous clinoradiological entity typically comprised of a clinical symptom including headache, seizures and visual disturbances, combined with MRI findings indicative of reversible posterior leukoencephalopathy and vasogenic edema. As PRES became increasingly recognized, atypical radiological phenotypes were also described; the unilateral and reversible diffusion restriction variants. We present here the report of a case of a 72 year old female patient with a personal history of inflammatory bowel disease and Adamantiades-Behcet's Disease (ABD) that presented a clinoradiological syndrome in the spectrum of atypical PRES, coinciding with the complication of ABD with the non-parenchymal variant of NBD. Though autoimmune disease has been proposed as an etiological factor of PRES, we are the first to our knowledge to specifically report a case of PRES in the setting of a first-onset NBD. Furthermore, we argue that in ABD, PRES may represent an intermediate, benign phenotype of NBD where endothelial dysfunction is transient, and thus the full spectrum of non-parenchymal NBD may not be developed.

Enhancement of cognitive functions by rice bran extract via regulation of ppar γ in neuroinflammatory alzheimer's disease mouse model

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Alzheimer's disease (AD) is a neurodegenerative disease for which currently there exists no effective therapy. Recent clinical trials of PPAR γ receptor agonists in AD patients revealed improvement in memory, representing a promising treatment for AD. Recent studies have demonstrated the protective effect of rice bran extract (RBE) on AD models. Moreover, Rice bran constituents, namely, polyunsaturated fatty acids and γ -oryzanol were recently considered as PPAR γ modulators. Accordingly, the effect of RBE on memory and cognition in a neuroinflammatory AD mouse model was examined. Furthermore, this study tested whether RBE improves cognition through modulating PPAR γ . Neuroinflammatory AD mouse model was developed by injecting LPS i.p (250 μ g/kg) for 7 consecutive days. Mice were administered by oral gavage for 21 days RBE (100mg/kg) or the known PPAR γ agonist pioglitazone (30mg/kg), or the PPAR γ antagonist GW9662 (3mg/kg) followed by RBE or pioglitazone. Mice were subjected to object recognition test, y-maze and water maze test. Additionally, PPAR γ DNA binding activity was measured in mouse brains. Results indicate a significant improvement of the spatial working and recognition memory by RBE in the LPS mouse model. Interestingly, the effect of RBE on memory was abolished in the group injected with PPAR γ antagonist before RBE treatment, indicating the important role of PPAR γ in the mechanism of action of RBE. Furthermore, PPAR γ DNA binding was increased by RBE and this effect was reversed by PPAR γ antagonist. These findings demonstrate that RBE improves cognition and its effects are correlated with its action on PPAR γ .

Sleep disorders and mild cognitive impairment

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Introduction: Mild cognitive impairment (MCI) is the transient stage between the normal old age and dementia. The transition from the normal aging in the MCI is sensitive. The observation of sleep changes can distinguish the healthy aging from dementia. Taking into consideration that the MCI diagnosis is based on neuropsychological evaluation, we must check to what extent sleep disorders contribute to the cognitive impairment of these people. Objective: The current literature review is going to analyze sleep disorders in people who were diagnosed with MCI. Methods: A systematic review of the existing literature was conducted in the following databases: PubMed, Embase and Medline. Key words: sleep disorders, mild cognitive impairment, elderly, AD. The articles were published from 2006 to 2016. Results: It is evident from the literature review, that the sleep disorders as one of the most common neuropsychological symptoms, are more frequent in patients who suffered from MCI compared with healthy elderly. On the top, their treatment may deter the onset of dementia. Conclusions: Sleep disorders are prevalent among the elderly diagnosed with MCI and neurodegenerative diseases. The determination of sleep changes could be transitive indicators in cognitive impairment or dementia. The disclosure of the relationship between sleep changes and changes in cognition is a gap in the literature in which future studies should investigate.

Distinguishing between working memory and inhibition impairment in dementia

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Dementia is often associated with impairments of both working memory and inhibitory control. However, it is unclear whether these are functionally distinct impairments. So far the eye-tracking studies of IC have relied heavily on studies that are based on the average scores from groups that were tested at a given time point. A detailed assessment of individual cases can address questions in relation to the dissociation of cognitive operations, which cannot be resolved by the average scores from a group of diverse patients. A key aim is to determine the value of eye-tracking in detecting early dementia. Are deficits of eye-tracking evident before impairments in traditional cognitive assessment in people with dementia? Do impairments of working memory and inhibitory control emerge at the same time in dementia? The patient group consisted of 18 patients with early dementia (13 males, 5 females). All patients underwent a detailed clinical history, physical/neurological examination and routine investigations. An old control group 18 healthy participants (8 males, 10 females) were volunteers from the local Lytham community. All OC participants underwent a detailed neuropsychological assessment. Tests for the dissociations of neurocognitive inhibitory control (anti-saccade) and working memory span were conducted with reference to the control sample using the revised standardized difference tests. Results: 33% patients from the original sample (N=17) met the Crawford and Garthwaite (2005) statistical criteria for a “strong” dissociation. Some patients revealed a preserved working memory capacity together with poor inhibitory control in the anti-saccade task. A longitudinal follow-up revealed that the defective inhibitory control emerged 12-months before the dementia was evident on the mini-mental state examination assessment. Other cases revealed a poor working memory together with a well-preserved level of inhibitory control. There is increasing evidence that people with early Alzheimer’s disease have subtle impairments in cognitiveinhibitory control that are often undetected by traditional cognitive assessments. We suggest that inhibitory impairment should be a focus of treatment, disease monitoring and assessment in pharmacological drug trials.

A unique pattern on memory testing in dementia screening predicts obstructive sleep apnea

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Objective: The Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) is used to screen for dementia. A unique pattern of Immediate Memory lower than Delayed Memory scores (IM<DM) predicted Obstructive Sleep Apnea (OSA), a potentially reversible cause of “dementia” in our Memory Care Clinic (MCC) patients. We reviewed the results for all patients evaluated in our MCC for a total of three years. Methods: A retrospective chart review of all patients seen in our MCC from December 2011 to December 2014 was completed. Those with the pattern of interest (IM<DM) were compared to those without the pattern for the presence of OSA. Results: A total of 191 patients fit the inclusion criteria of completing the RBANS during the period of the study. Of the total group, 81 (42%) displayed the IM<DM pattern; 54 of these patients had been or were subsequently tested for OSA and 35 were positive (65%). The average age of the positive group was 74 and 60% were women. A previous study showed that Body Mass Index (BMI) was not significantly different between the two groups. Conclusions: OSA is a known risk factor for cognitive dysfunction. It is a potentially treatable cause of memory loss and can be clinically silent. This study shows that a unique pattern (IM<DM) on the RBANS commonly used at Memory Clinics can identify a group of patients who can be evaluated for this common and remediable condition.

Involvement of nitric oxide in aluminium neurotoxicity: effects of L-NAME are protective and dose-dependent

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Undoubtedly, aluminium is a very harmful substance when enters the human body, which happens primarily unintentionally from the environment. When accumulated in the brain, it is involved in severe damages found in chronic neurodegenerative diseases, including Alzheimer's disease. Knowing the pathogenetic mechanisms of these damages could improve prevention/treatment of aluminium-induced neurotoxicity. Since the important role of nitric oxide (NO) in these processes, in our research, just prior to aluminium chloride, a nonselective nitric oxide synthase inhibitor N ω -nitro-L-arginine methyl ester (L-NAME) was applied in the hippocampus of Wistar rats with three doses. Effects of both substances were examined clinically by the active avoidance test and biochemically by measuring cytochrome c oxidase and glucose-6-phosphate dehydrogenase activity in the forebrain cortex, basal forebrain, striatum and hippocampus. It was demonstrated that inhibition of NO synthesis protects animals against aluminium neurotoxicity. That was registered through improved behaviour, or even its reversion, i.e. the decreased number of active avoidance responses induced by aluminium chloride reached the values of control animals by the pre-treatment with L-NAME. Also, aluminium-induced disrupt of glucolysis and mitochondrial oxidative phosporilation was statistically significantly improved with the highest dose of L-NAME. Neuroprotective effects of L-NAME against aluminium neurotoxicity was shown to be dose-dependent.

Compare therapy of Alzheimer's disease with cholinesterase inhibitor (Aricept or Nivalin) plus akatinol-memantine

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Abstract BACKGROUND/OBJECTIVE: To compare the effectiveness of combination therapy with cholinesterase inhibitors (ChEI) plus Akatinol-Memantine in all AD patients and in older AD patients (age 75 years). **METHODS:** The Akatinol-Memantine Study was used to compare the clinical effects of combination therapy of Aricept plus Akatinol-memantine (n = 19) or Nivalin plus Akatinol-memantine (n = 16) in all AD patients, and in older AD patients separately, at 6 months with ChEI only monotherapy, and at 2, 4, and 6 months after addition of Akatinol-memantine to the treatment schedule (8 months total). **RESULTS:** The addition of Akatinol-memantine resulted in stabilization of the Mini-Mental State Examination scores and Hasegawa dementia rating for 6 months, and then significantly declined at 8 months in both subgroups. Frontal assessment battery (FAB) declined significantly at 8 months after Akatinol-memantine addition in the Aricept subgroup, while the Nivalin subgroup significantly improved at 4 months. Affective functions were well preserved after Akatinol-memantine addition until 8 months, except for the apathy scale at 8 months after Akatinol-memantine addition in the Nivalin subgroup. The combination therapy of Aricept plus Akatinol-memantine was better for apathy in older AD patients, and Nivalin plus Akatinol-memantine was better for cognitive functions. **CONCLUSIONS:** The addition of Akatinol-memantine stabilized cognitive scores much more for 4 months and affective scores for 8 months in the Aricept subgroup. Additionally, Akatinol-memantine significantly improved FAB at 4 months in the Nivalin subgroup although apathy scale became significantly worse at 8 months.

Association between serum haptoglobin and the pathogenesis of Alzheimer's disease

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Objective: Haptoglobin (Hpg) is known to have several functional properties, including antioxidant and anti-inflammatory activities. In addition, it has been shown that the pathogenesis of neurodegenerative disorders, such as Alzheimer's disease (AD), involves inflammation as well as oxidative stress. However, evidence suggesting an association between the serum Hpt level and AD is lacking. Therefore, we conducted this study in order to investigate whether serum Hpg is associated with AD. Methods: We compared the serum Hpg levels of 121 patients with newly diagnosed AD, 58 patients with Parkinson's disease (PD) and 43 healthy controls. We also evaluated the relationship between the severity of cognitive impairment in patients with AD and the serum Hpg level. Results: The mean serum Hpg level of the patients with AD was significantly higher than that of the healthy controls ($p=0.042$), although it was not significantly different from that observed in the PD group ($p=0.613$). We also found a significant positive association between the serum Hpg level and the severity of cognitive impairment, as measured using several neuropsychological tests, in the patients with AD. The odds ratio (95% confidence interval) of the patients with AD grouped according to the Hpg level was 2.417 (95% confidence interval=1.134-5.149). Conclusion: We observed a significantly higher mean serum Hpg level among the patients with AD compared to the healthy controls. These results support the hypothesis that oxidative stress and neuroinflammatory reactions play a role in the pathogenesis of AD.

The impact of music therapy as a method of treatment in patients with alzheimer's disease.

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The notion of a specialized and independent memory system for music in the human brain is supported in several studies. Explicit memory for music differs between healthy people, patients with dementia and patients with Alzheimer's disease. Alzheimer's disease is the most common cause of degenerative dementia including progressive cognitive and behavioural alterations. Musical memory is the last to be impaired in comparison to other memory regions of the brain in the very late stages of the disease. Patients' poor response to medications has led to the development of non-pharmacological methods of treatment, especially music therapy due to the preservation of musical memory. Several studies show that music stimulation leads to the improvement of explicit memory, linguistic skills, and behavioural, emotional and social manifestations, as well as to the enhancement of motor learning and physical activity and an overall improvement of quality of life. Our pilot study in the Neurophysiology Laboratory of the University of Cyprus Medical School including neurophysiological tests in healthy young and elderly people and in patients with dementia and Alzheimer's disease aims to determine the differences in cognitive functions between these groups. Understanding these differences contributes to the development of music therapy as a simple and safe supplementary method of treatment with long-lasting effects. Our results support the further investigation of the cognitive alterations during aging and the potential neural mechanisms associated with music therapy's beneficial effects in patients with Alzheimer's disease. Keywords: music therapy, memory, Alzheimer's disease.

Cognitive impairment in multiple sclerosis: recent findings

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Cognitive impairment is one of the many symptoms in multiple sclerosis, which plays a critical role in the patient's everyday life. The most common cognitive deficits appear in information processing speed, attention, memory, learning, and executive functions. After years of research there aren't clear instructions in the assessment, which creates problems in the therapeutic process. This article is a literature review of the recent findings in deficits in MS patients and in- neuropsychological tests' validity and reliability. Fifty seven articles published from 2006 to 2016 were selected. Most studies confirmed declining deficits in the domains that were mentioned in previous literature in various MS subtypes, but also in social cognition and emotion recognition. The examination of various already established cognitive tests in the detection of cognitive impairment and deterioration showed that SDMT (Symbol Digit Modalities Test) is the strongest measuring tool for IPS and working memory alongside with PASAT (Paced Auditory Serial Addition Task). The short version of BRB (Selective Reminding Test, PASAT-3 and SDMT) also had great results and covered many cognitive domains. CVLT-II (California Verbal Learning Test-II) was a sensitive test for verbal memory while BVMT-R (Brief Visual Spatial Memory Test-Revised) was a good screening tool for visual memory. Verbal fluency/executive functions can be assessed with WLG (Word List Generation). MSNQ (Multiple Sclerosis Neuropsychological Questionnaire) is recommended for everyday functioning and TASIT (The Awareness of Social Inference Test) for social cognition screening.

Apolipoprotein e ϵ 4 allele frequency in Korean patients with parkinson`s disease dementia

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Background: It has been well known that the APOE ϵ 4 allele is a strong risk factor in Alzheimer`s disease (AD) and occurs at an increased frequency in dementia with amyloid pathology. However The clinical significance of the apolipoprotein E (Apo E) 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 Apo E 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. *Method:* Forty patients participated in the study, Twenty patients with PDD and 20 age matched healthy controls. The Apo E genotype was determined by the polymerase chain reaction (PCR) and allele specific hybridization using the Apo E typing test kit. *Results:* The Apo E ϵ 4 allele frequency in the PDD group was 35% and was significantly higher than those of normal controls (15%) ($p < 0.05$). The Apo E ϵ 4 carrier frequency in the PDD group was 60%, and also significantly higher than those of normal controls (30%) ($p < 0.05$). The Apo E ϵ 3 allele was the most frequent genotype in Korean population generally in this study. *Conclusion:* These results that the elevated Apo E 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.

Does personality influence the efficacy of art on pain and mood in patients with alzheimer's disease? Evidence from a randomized controlled trial

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Art interventions are often proposed to patients with Alzheimer's disease (AD) and patients with chronic pain. Personality was demonstrated to play a role in the clinical evolution of both AD and chronic pain. This study aimed at assessing the role of personality on the efficacy of art intervention on pain and mood in patients with mild AD who also complaint about chronic pain. Methods: Fifty mild AD patients were randomized to a 12-week art intervention (painting or choral singing). Personality was assessed with the Big Five Inventory, identifying 5 traits according to the Big Five Model (Neuroticism, Openness, Conscientiousness, Agreeableness and Extraversion). Chronic pain, anxiety and depression were assessed before, just after intervention and 1 month later. The relationship between personality traits and the evolution of these three measures were assessed with mixed linear models. Results: The only significant change after art interventions was associated with neuroticism: a high level of neuroticism was associated with a paradoxical increase of chronic pain. In contrast, in patients with lower levels of neuroticism, pain decreased significantly after art interventions (Numeric Scale: $F=9.63$; $p=0.002$; Simplified Visual Scale: $F=5.92$; $p=0.016$; Brief Pain Inventory: $F=6.47$; $p=0.012$). Moreover, the evolution of mood disorders after art sessions was not influenced by personality. Conclusion: The present findings suggest some efficacy of art interventions in patients with lower neuroticism, but not for patients with a high level of neuroticism. They reveal the importance to identify these patients and to propose them alternative care.

Dementia in the presence of RBD is sufficient for diagnosis of probable DLB

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REM sleep behavior disorder (RBD) is characterized by dream-enacting behaviors with excessive motor activity. It has long been known that RBD precedes the development of neurodegenerative syndromes, especially synucleinopathies such as Parkinson disease (PD), multiple system atrophy (MSA), and dementia with Lewy bodies (DLB). RBD occurs in up to 70% of DLB patients and detection of RBD in patients with neurodegenerative dementia may suggest a Lewy body pathology¹. Third report of DLB consortium added REM sleep behavior disorder to the suggestive features of DLB diagnosis in 2005. RBD has been found to represent a red flag for progressing cognitive impairment^{2,3} and can precede other aspects of synucleinopathies by up to half a century⁴. In a study of patients with autopsy-confirmed DLB with low to high likelihood, the presence of RBD in the clinical history was associated with a higher likelihood of DLB pathology and less severe Alzheimer-related pathology in the medial temporal lobes, whereas absence of RBD was characterized by greater hippocampal and lateral Temporoparietal atrophy on MRI and increased phospho-tau burden⁵. large cohort study of 174 patients with idiopathic RBD showed that the risk of developing a neurodegenerative syndrome from the time of idiopathic RBD diagnosis was 90.9% at 14 years⁶. In only a 4 year follow up, about third of patients (n=51) converted to DLB or PD⁶. There is a strong belief that RBD, when diagnosed by Polysomnogram, might be the strongest risk factor for DLB when compared with other signs^{7,8}. This body of evidence calls upon the experts to revisit the DLB diagnostic criteria and to consider RBD as one of the core features of DLB. Basically, RBD in the presence of dementia represents Probable Dementia with Lewy bodies.

The variation in the relationship between memory, cognitive control and theory of mind in two groups of elderly; patients with mild cognitive impairment and patients with vascular risk factors.

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Several studies have linked non-diagnosed vascular pathology with cognitive impairment. It is reasonable to maintain that since vascular disease affects the brain, it also affects cognitive functioning especially functions supported by the frontal lobes. The theoretical approach of the “vascular hypothesis of cognitive aging” posits hypertension, hyperlipidemia, and diabetes mellitus as basic risk factors for vascular disease. A step further in regards to cognitive decline, the term ‘Mild Cognitive Impairment (MCI)’ was introduced to describe a subtle decline in cognition identified as a first ‘indicator’ of the dementia trajectory. Besides the well established memory deficits, many patients with MCI deal with problems in executive functions or cognitive control processes while in the more recent literature, we come across studies on Theory of Mind (ToM) in MCI. The present study aims to investigate the differences of older adults having vascular risk factors and MCI patients in regards to the pattern of the relations between cognitive control, memory and Theory of Mind. The sample consisted of two groups (VRF and MCI) of older adults ($n = 50$), matched for gender, age and educational level. The findings indicated that complex ToM as indirect speech understanding was at a significantly lower level in MCI patients, as compared to community dweller VRF group. Moreover, MCI patients had a serious deficit in recruitment of combined executive functions in order to support indirect speech understanding.

Seronegative neuromyelitis optica spectrum disorders, challenges in diagnosis and management, a case report

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24 year old female presented with few days history of pins and needles on her right toes and bilaterally on her fingers. She has background of chronic back pain and anxiety depression. A week later she presented to A+E with severe back pain and weakness on her right leg and left arm. A+E performed an assessment and she was reassured that her symptoms did not appear to be organic so she was discharged. Two weeks after the initial complaint she presented with severe weakness of her right leg, left arm and urinary retention. She was admitted and despite the rapid progression of her symptoms she appeared to have a functional element that made the diagnosis challenging. Two days later, after the presentation in the acute neurology ward she had progressed to being tetraplegic, with hard signs suggestive of spasticity. The MRI of her neuroaxis depicted extensive transverse myelitis sparing the brain. She was treated with intravenous methylprednisolone on the presumption that this is neuromyelitis optica but she did not show any signs of improvement. Her AQP4 and MOG antibodies returned negative but we endeavoured to treat her with plasma exchange. After the third plasma exchange she demonstrated signs of recovery on her upper limbs and after completion of the immunotherapy she started showing some improvement on the lower limbs as well. This very didactic case demonstrates the challenges that can be faced when there is a significant functional overlay and no serological confirmation, furthermore it depicts the dilemmas in treating immunoinflammatory conditions of uncertain aetiology.

Acute retinal necrosis (arn) following rituximab therapy in a neuromyelitis optica (nmo) patient

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Background: Rituximab is the main disease-modifying treatment for Neuromyelitis Optica (NMO). It can be associated with severe complications. **Methods:** Case report: An NMO patient who developed Acute Retinal Necrosis (ARN) while on rituximab treatment. **Results:** A 36-year-old male was diagnosed with NMO five years prior to presentation. Treatment with rituximab (1g IV every 6 months) for the past 4 years, resulted in clinical remission. In September 2016 the patient presented with sudden loss of vision in the left eye (20/50) with associated mydriasis. Ophthalmologic examination was consistent with ARN. Cranial and orbital MRI revealed thickening and edema of the left optic nerve extending to adjacent chiasm, without contrast-enhancement. CSF PCR for viruses and toxoplasma were negative. He was also seronegative for HIV. PCR for HSV1 was positive in aqueous humor biopsy. IV acyclovir (750 mg three times daily) was given for 14 days; he was then switched to oral valaciclovir (1500 mg daily) for 3 months. Prednisone (60mg/d) was added. The patient had a remarkable recovery of visual acuity in the affected eye (20/25) at four months after symptom onset. **Conclusions:** ARN is a rare viral pan-uveitis that can be induced by rituximab treatment. In NMO patients on chronic treatment with this potent immunosuppressive agent, viral ARN should be considered when unilateral visual complaints occur. Clinicians should maintain a high index of suspicion to properly distinguish ARN from other NMO-related causes of visual loss, such as optic neuritis, so that prompt treatment is initiated.

The outcome of ganglion clipping in hyperhidrosis and accidental wrong clipping

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Objective: The definite treatment for hyperhidrosis and facial blushing remains on surgery. This study is to assess the outcome, side effects and convey the concept of reflex sweating (RS) after sympathetic blockade (ESB) for the disorder. Methods: Between Aug 2001 and Dec 2003, data from 106 patients who underwent thoracoscopic ESB with clipping for various sympathetic disorders were retrospectively reviewed. In total, 69 patients had hyperhidrosis palmaris (HP), 30 hyperhidrosis craniofacialis (HCF) and 7 facial blushing (FB) were collected. Results: For HP, after T4 blockade, all successful with no reflex sweating. For HCF, after T3 blockade, all successful with mild reflex sweating. For FB, after T2 blockade, all successful with one patient intolerable reflex sweating (clipping reversed). There was no recurrence. Accidental finding of 4.4% of patients were unintentionally unilaterally clipped at wrong ganglion level→different feeling between two sides→confirmed by chest radiography→reclipped. Conclusions: The blocked level under the principle of Lin-Telaranta classification is of high successful rate, with very low side effects. Even an experienced surgeon would intervene the wrong ganglion and clipping provides a good marker for postoperative assessment.

The influence of intensive upper-extremity training on endurance and cardiac autonomic regulation system of children with unilateral cerebral palsy: a self-control clinical trial

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Background: An intensive hybrid program improves upper extremity function as well as walking endurance of children with unilateral cerebral palsy (UCP). Endurance improvement may be associated with the cardiac autonomic regulation system (CARS) adaptation, known to be impaired among these children. **Objective:** To examine the influence of an intensive hybrid program on CARS, walking endurance and the correlation with upper extremity function of children with UCP. **Methods:** 24 children aged 6-10 years with UCP participated in a hybrid program, 10 days, 6 hours per day. Data were collected pre-, post- and 3-months post-intervention. Main outcome measures included the Polar RS800CX for heart rate (HR) and heart rate variability (HRV) data, the 6-Minute Walk Test (6MWT) for endurance, and the Assisting Hand Assessment (AHA) and Jebsen-Taylor Test of Hand Function (JTTHF) for bimanual and unimanual function. **Results:** A significant reduction in HR and an increase in HRV at post- and 3-month post-intervention was noted ($\chi^2_{2}=8.3$, $p=0.016$) along with a significant increase in 6MWT with a median increase of 81 meters ($\chi^2_{2}=11.0$, $p=0.004$) at the same interval. A significant improvement was noted in unimanual and bimanual performance following the intervention. **Conclusions:** An intensive hybrid program effectively improved CARS function as well as walking endurance and upper extremity function in children with UCP.

Antiepileptic drug effects on sex-steroid hormones in women with epilepsy

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Introduction: Women with epilepsy are at risk for reproductive health dysfunction. Alterations in hormone levels are a direct effect of epileptic discharges, both in animals and humans. Antiepileptic drugs (AEDs) are known to have endocrine side effects in women with epilepsy. Distinguishing the side effects of antiepileptic drugs (AEDs) from the many other factors that influence the patients can be difficult. Methods: Sex-steroid hormones were evaluated in 20 reproductive-aged women with epilepsy receiving an AED in monotherapy. None of the patients had been diagnosed with an endocrine disorder before starting AED treatment or had used drugs that may interact with endocrine function. 10 women were treated with levetiracetam (LEV) and 10 with lamotrigine (LTG) for at least 2 years. Estradiol (E2), testosterone (T), dehydroepiandrosterone (DHEA), sex hormone-binding globulin (SHBG) were evaluated in follicular phase and progesterone (P) in luteal phase of menstrual cycle. Results: E2 levels were normal in all women. T levels were abnormal in 5 (25%) patients: elevated in 4 (2 on LEV, 2 on LTG) and lowered in 1. DHEA levels were elevated in 5 (25%) patients (2 on LEV, three on LTG). SHBG levels were elevated in 4 (20%) patients (2 on LEV, 2 on LTG), P levels were lowered in 9 (45%) patients (6 on LEV, 3 on LTG). Any abnormalities were found in 10 (50%) women (6 on LEV, 4 on LTG). Conclusion: These preliminary results indicate that new AEDs may alter sex-steroids levels in women with epilepsy.

Acoustic range magnetic stimulation improves learning and memory function in genetically prone to audiogenic seizure rats

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Deterioration of the cognitive function is associated with epilepsy. Antiepileptic drugs lead to memory damage. Therefore, we decided to study effects of acoustic range magnetic stimulation (MS) on learning and memory functions in genetically prone to audiogenic seizure rats (GEPRs) and inbred white rats (n=14) by the use of a multi-branch maze. For this task a part of GEPRs and a part of inbred rats were radiated with MS. MS – 10000 Hertz frequency, 1,5 m/Tesla, during 5 days, 20 min per day changed behavioral seizure manifestations in GEPRs. MS decreased the number of errors (getting in the deadlock branch) that the rat was making to reach the destination and the time needed for passing the maze in both groups, especially in GEPRs. The time needed to reach the destination was less in GEPRs ($p \leq 0.05$) compared to inbred ones. We assumed that MS decreases anxiety and enhances exploratory activity of the GEPRs. Audiogenic seizure rats have damaged memory. MS on these rats improve their memory and this may lead to a new treatment for memory improvement. In our study we showed the positive effects of MS on learning and memory functions. Therefore, acoustic range MS can apply partial or complete suppression of seizures and improvement of memory function. These results provide further insights for a better understanding of the fundamental neurobiology of memory. Research was supported by FR /257/7-270/14

How the rate of titration of lamotrigine influence to its tolerability and frequency of side effect and is it really optimal?

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The prescription lamotrigine without titration significantly increases the risk of adverse reactions - most often a skin rash, which is the most common reason for early discontinuation of this drug. But in the available literature there is no clear substantiation of the rate of titration of lamotrigine suggested in the instructions. We studied the tolerance and safety of lamotrigine in 186 patients with epilepsy who have used the schemes more rapid titration, depending on additionally using AED. The drug as a first monotherapy was administered to 27 patients, 106 patients were used lamotrigine as an additional AED (without using valproic acid), and 43 - lamotrigine was added to valproic acid. The age of study participants was 18 to 54 years. Patients in history with a skin rash associated with the use of medicines or other allergic reactions associated with the medication, the study was not included. Monitoring of patients was carried out monthly for 12 weeks after lamotrigine prescription and dose beginning. For further analysis, we considered the frequency of such side effects as skin rashes, dizziness, nausea, vomiting and sleep disturbances as the most frequent for lamotrigine using. The frequency of adverse events in the study were compared with data from metaanalyses and multicenter clinical trials. Comparison of survey data with that obtained in the sources of the literature showed that increasing the speed of the titration of lamotrigine twice does not affect the increase in the frequency of more often side effects lamotrigine and the percentage of patients requiring drug discontinuation because of their appearance, as for all patients which used lamotrigine and as for separate clinical groups.

Is overdiagnosing of epilepsy a common trend?

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Epilepsy is a neurological disease which affects around 0.5-1.0% of the population. Approximately 10% of the population goes through at least one seizure (febrile, metabolic, toxic, withdrawal etc.), but are not diagnosed with epilepsy. Further obstacle to correct diagnosis is the vastness of different types, including nonconvulsive attacks e.g., absence seizures. Thorough medical history correlated with the type of seizures present, supported by diagnostic research (including electroencephalography), plays a crucial role in proper diagnosis. In this study, we present only selected clinical cases of patients hospitalized in our department, who were earlier diagnosed with epilepsy which we could not confirm. In the majority of these cases, we diagnosed migraine with visual aura. In one case a patient was formerly diagnosed with complex partial seizures secondarily generalized seizures. The second case was previously diagnosed with absence seizures. In our opinion, clinical signs in both patients suggested psychogenic seizures. Conclusion: Even though this is not a population study but a presentation of selected cases, we have come to realize that overdiagnosing of epilepsy is an existing trend. There seems to be a necessity for more rigorous use of current guidelines or even a creation of new, more detailed ones, to enable correct diagnosis of epilepsy.

EPILEPSY IN PATIENTS WITH DOWN SYNDROME

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Subjects and Methods: At the period 2000-2016 at the Department of Psychoneurology N2, Russian Children Clinical Hospital and Department of Child Neurology, Neurosurgery and Medical Genetics, Russian National Research Medical University were observed 11 patients with Down syndrome (7 boys and 4 girls). Nine children with classic variant (47,XX,+21) and one boy with mosaicism (46, XX/47,XX,+21). **Results:** Age of epilepsy onset varies from 1,5 month to 4 years (8 month at the average), in 10 from 11 patients (90,9%) before 1 year of life. The most part of patients with DS presented West syndrome (n=7, 63,6%), 3 patients with Markand-Blume-Ohtahara syndrome or severe epilepsy with multifocal independent spike foci – SE-MISF (27,3%) and one girl with focal frontal lobe epilepsy, Lennox-Gastaut-like phenotype (9,1%). West syndrome was characterized by flexor and flexor-extension tonic spasms, serial and single. SE-MISF characterized of combination of tonic spasms, ophthalmo-tonic, myoclonic and versive tonic seizures. Lennox-Gastaut-like phenotype – with pseudo-generalized tonic axorhizomelic and myoclonic seizures. Clinical remission was observed in 6 of 11 patients with DS (54,5%), significant decreasing of seizures (75%) – in 4 (36,4%) of children and moderate decreasing - in 1 (9,1%). **Conclusion:** Epileptic seizures in DS predominantly had manifestation in infancy (90,9%). Epilepsy had predominantly good prognosis (complete remission of seizures in 54,5% and significant decreasing of seizures – in 36,4% of cases). The most effective drugs were valproates in monotherapy and in combination with ethosuximide, lamotrigine, benzodiazepines and barbiturates.

Surgical treatment of nonlesional neocortical epilepsy

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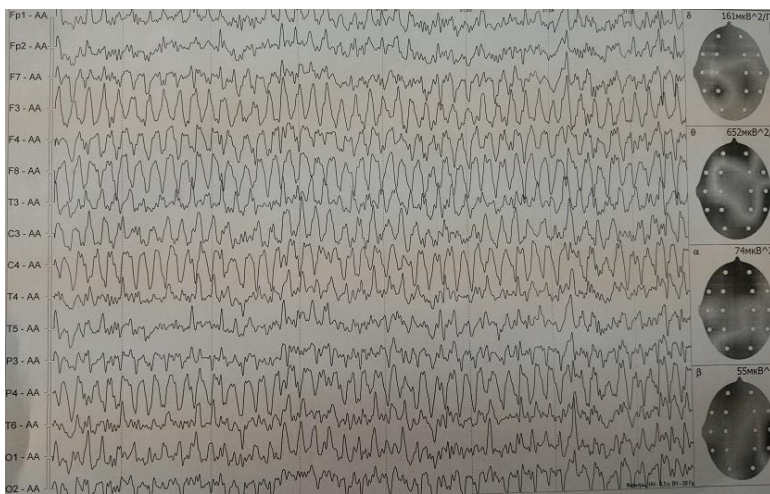
Objective: The proportion of surgery for nonlesional neocortical epilepsy has recently increased, with a decrease in surgery for mesial temporal lobe epilepsy. The objective of this study was to evaluate the long-term surgical outcome and to identify possible prognostic factors in patients with nonlesional neocortical epilepsy. **Methods:** We included 109 consecutive patients without MRI-identifiable lesions who underwent focal surgical resection for drug-resistant neocortical epilepsy. Follow-up information for at least 10 years was available for all but one patient. Univariate and standard multiple logistic regression analyses were performed to identify the predictors of surgical outcomes, and a generalized estimation equation model was used for the longitudinal multiple logistic regression analysis of up to 21 years of follow-up. **Results:** At 1 year after surgery, 59 out of 109 patients (54.1%) achieved seizure freedom, and 64 out of 108 (59.3%) patients achieved seizure freedom at the last follow-up. Only 11 out of 108 patients (10.2%) experienced definite changes in postoperative seizure status. Localizing patterns in functional neuroimaging, concordant results in presurgical diagnostic evaluations, the presence of aura, and complete resection of areas of ictal onset with frequent interictal spikes during the intracranial EEG study were favorable surgical outcome predictors. **Conclusion:** Our study showed that nearly 60% of patients with nonlesional neocortical epilepsy achieved long-term seizure freedom, and that changes in postoperative seizure status were rarely observed. Several predictors of favorable surgical outcomes were identified, which can help select optimal candidates for surgical treatment among patients with nonlesional neocortical epilepsy.

Psychoanalytic treatment of idiopathic epilepsy

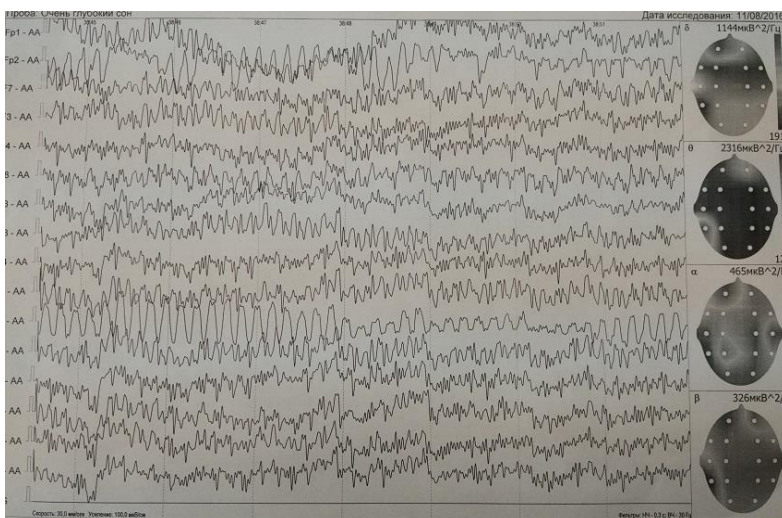
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Idiopathic epilepsy are common at different ages and varied in clinical manifestations. However, they all have common morphological substrate: a violation of the interaction of the hippocampus and the amygdala, as a structure who are responsible for switching of consciousness a variety of clinical manifestations helps the diagnosis of epilepsy, but does not play a fundamental role in the treatment. We affirm that idiopathic epilepsy have mixed etiopathogenesis: they are caused by primary or acquired weakness amigdalo- hippocampal communication and psychological reasons. When the drug provides 100% control of seizures, - we begin psychoanalytically oriented psychotherapy. This type of therapy is aimed at the realization of unconscious processes, including - aggression, which plays a key role in causing excitotoxicity amygdala. Also, this type of therapy affects the re-evaluation of the meaning of experienced events that defines the operation of the hippocampus in the formation of long-term memory, stability of mind in situations of unbearable levels of sensory processing and experiences while sleeping. The treatment process includes regular testing and assessment of the patient's condition changes affective reactions, which allows you to determine when you can begin to undo AEP. Cancel preparations made gradually, for an average of 1-1.5 years. Changing control affect allows us to cancellation of a reliable product. Clinical example. Changed EEG pattern. EEG at the beginning of treatment.



Last EEG



Stopped seizures

The effect of b12 deficiency in adult seizure occurrence

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400 pg/ml). Patients with known epilepsy, antiepileptic drug treatment, alcohol abuse, metabolic, cognitive or psychiatric disorders were excluded. Both groups were submitted to brain imaging. Correlation between the participants' variables and quantitative electroencephalographic (QEEG) values was estimated. Re-evaluation was repeated three months after B12 treatment. Results Patients, with B12 200 pg/mL, showed statistically significant differences of their QEEG parameters both in relation to the control and second patient group. An increase of paroxysmal EEG activity was observed and 7% of them presented seizures. EEG recordings of the 2nd group were characterized by pronounced theta rhythms in the fronto-temporal regions and alpha3/alpha2 frequency ratio reduction, correlating with detected memory deficits. Restoration of EEG abnormalities was noted 3 months after intramuscular cobalamin supplementation. Conclusion B12 insufficiency appears to be associated with EEG rhythm alterations. Evaluation of B12 serum levels should be undertaken in differential diagnosis of late onset seizures"

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Cobalamin's contribution to normal nervous system functioning is well known. While extensive references exist concerning neuro-psychiatric disorders caused by B12 deficiency, only a few pertain to epileptic seizures especially in adulthood. 400 pg/ml). Patients with known epilepsy, antiepileptic drug treatment, alcohol abuse, metabolic, cognitive or psychiatric disorders were excluded. Both groups were submitted to brain imaging. Correlation between the participants' variables and quantitative electroencephalographic (QEEG) values was estimated. Re-evaluation was repeated three months after B12 treatment. Results Patients, with B12 200 pg/mL, showed statistically significant differences of their QEEG parameters both in relation to the control and second patient group. An increase of paroxysmal EEG activity was observed and 7% of them presented seizures. EEG recordings of the 2nd group were characterized by pronounced theta rhythms in the fronto-temporal regions and alpha3/alpha2 frequency ratio reduction, correlating with detected memory deficits. Restoration of EEG abnormalities was noted 3 months after intramuscular cobalamin supplementation. Conclusion B12 insufficiency appears to be associated with EEG rhythm alterations. Evaluation of B12 serum levels should be undertaken in differential diagnosis of late onset seizures"

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B12 serum levels should be undertaken in differential diagnosis of late onset seizures" Two groups of 25 patients each (mean age 67 years) were investigated; one with B12 deficiency (serum levels 200 pg/ml); the other with B12 levels in the gray zone of 200- 400 pg/ml. A matching healthy control sample was included (B12 400 pg/ml). Patients with known epilepsy, antiepileptic drug treatment, alcohol abuse, metabolic, cognitive or psychiatric disorders were excluded. Both groups were submitted to brain imaging. Correlation between the participants` variables and quantitative electroencephalographic (QEEG) values was estimated. Re-evaluation was repeated three months after B12 treatment. 400 pg/ml). Patients with known epilepsy, antiepileptic drug treatment, alcohol abuse, metabolic, cognitive or psychiatric disorders were excluded. Both groups were submitted to brain imaging. Correlation between the participants` variables and quantitative electroencephalographic (QEEG) values was estimated. Re-evaluation was repeated three months after B12 treatment. Results Patients, with B12 200 pg/mL, showed statistically significant differences of their QEEG parameters both in relation to the control and second patient group. An increase of paroxysmal EEG activity was observed and 7% of them presented seizures. EEG recordings of the 2nd group were characterized by pronounced theta rhythms in the fronto-temporal regions and alpha3/alpha2 frequency ratio reduction, correlating with detected memory deficits. Restoration of EEG abnormalities was noted 3 months after intramuscular cobalamin supplementation. Conclusion B12 insufficiency appears to be associated with EEG rhythm alterations. Evaluation of B12 serum levels should be undertaken in differential diagnosis of late onset seizures" Results: 400 pg/ml). Patients with known epilepsy, antiepileptic drug treatment, alcohol abuse, metabolic, cognitive or psychiatric disorders were excluded. Both groups were submitted to brain imaging. Correlation between the participants` variables and quantitative electroencephalographic (QEEG) values was estimated. Re-evaluation was repeated three months after B12 treatment. Results Patients, with B12 200 pg/mL, showed statistically significant differences of their QEEG parameters both in relation to the control and second patient group. An increase of paroxysmal EEG activity was observed and 7% of them presented seizures. EEG recordings of the 2nd group were characterized by pronounced theta rhythms in the fronto-temporal regions and alpha3/alpha2 frequency ratio reduction, correlating with detected memory deficits. Restoration of EEG abnormalities was noted 3 months after intramuscular cobalamin supplementation. Conclusion B12 insufficiency appears to be associated with EEG rhythm alterations. Evaluation of B12 serum levels should be undertaken in differential diagnosis of late onset seizures" Patients, with B12 200 pg/mL, showed statistically significant differences of their QEEG parameters both in relation to the control and second patient group. An increase of paroxysmal EEG activity was observed and 7% of them presented seizures. EEG recordings of the 2nd group were characterized by pronounced theta rhythms in the fronto-temporal regions and alpha3/alpha2 frequency ratio reduction, correlating with detected memory deficits. Restoration of EEG abnormalities was noted 3 months after intramuscular cobalamin supplementation. Conclusion B12 insufficiency appears to be associated with EEG rhythm alterations. Evaluation of B12 serum levels should be undertaken in differential diagnosis of late onset seizures" Conclusion: 400 pg/ml). Patients with known epilepsy, antiepileptic drug treatment, alcohol abuse, metabolic, cognitive or psychiatric disorders were excluded. Both groups were submitted to brain imaging. Correlation between the participants` variables and quantitative electroencephalographic (QEEG) values was estimated. Re-evaluation was repeated three months after B12 treatment. Results Patients, with B12 200 pg/mL, showed statistically significant differences of their QEEG parameters both in relation to the control and second patient group. An increase of paroxysmal EEG activity was observed and 7% of them presented seizures. EEG recordings of the 2nd group were characterized by pronounced theta rhythms in the fronto-temporal regions and alpha3/alpha2 frequency ratio reduction, correlating with detected memory deficits. Restoration of EEG abnormalities was noted 3 months after intramuscular cobalamin supplementation. Conclusion B12 insufficiency appears to be associated with EEG rhythm alterations. Evaluation of B12 serum levels should be undertaken in differential diagnosis of late onset seizures" B12 insufficiency appears to be associated with EEG rhythm alterations. Evaluation of B12 serum levels should be undertaken in differential diagnosis of late onset seizures.

Non convulsive electric status in a pregnant patient

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Introduction: Pregnant women comprise 25% of patients with epilepsy. Most of them require long-term treatment with AED. NCSE accounts for 4-25% of cases with SE. ESE constitutes 35-40% of cases of NCSE. Here we present the case of a pregnant with NCSE presented with psychotic symptoms during hospitalization makes ESE SE followed by the NCSE. *Clinical case:* the case of a 32 years old woman, in 33-34 week of pregnancy known for Epilepsy F-T from many years, treated with VPA which was interrupted before 11 months. The patient presented to the emergency with frequent behavior psychotic left front-parietal crises partial, without loss of consciousness, mood swings, ramp head right and difficulties to communicate, lasting several minutes. During the first day the patient enters the SE for about 4 h and was treated with IV Phenytoin. On the second day of hospitalization was significantly improved but the situation electrically ESE EEG results. Phenytoin treatment continues according to the protocol of Lamotrigin start. On the 5th day patient was seizure free and improvement of EEG track is observed. *Conclusion:* In women with epilepsy condition can deteriorate during pregnancy. NCSE can cause psychosis-like behavior. Hormonal changes during pregnancy crisis explain clinical presentation. ESE cases are very rare and more in pregnancy. Management of women with epilepsy in the perinatal period remains a challenge in medicine.

Epilepsy and pregnancy - which antiepileptic drug should we choose?

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Women with epilepsy have a slightly higher risk for some pregnancy and birth complications and require increased surveillance during pregnancy. Although two of three women with epilepsy remain seizure free throughout pregnancy, antiepileptic drugs (AEDs) dosages may need to be adjusted and therapeutic drug monitoring should be performed, at least every 4 weeks. Due to pharmacokinetic changes during pregnancy, the most pronounced decline in serum concentrations is seen for AEDs eliminated by glucuronidation, in particular lamotrigine (LTG). Consequently, the risks for uncontrolled seizures during pregnancy need to be balanced against potential teratogenic effects of AEDs. AED pregnancy registries continue to confirm that valproate (VPA) poses a significantly increased dose-dependent risk of structural and cognitive teratogenesis, ranging from 5.6% (750mg/day) to 24.2% (1500mg/day). Phenytoin (PHT), phenobarbital (PB) and topiramate (TPM) likely confer an intermediate risk of congenital malformations. Data thus far suggest that LTG, oxcarbazepine (OXC) and levetiracetam (LEV) are associated with a relatively low risk for both anatomic and developmental adverse effects. Accordingly, women with epilepsy should be treated with a low-dose monotherapy during pregnancy and VPA should be avoided. Supplementary folic acid (5 mg daily dose) is recommended, because this lowers the risk of cognitive teratogenicity. Third-trimester vitamin K supplementation has been suggested for women taking enzyme-inducing AEDs (eg. CBZ, PHT, PB), based on a concern for increased risk of intracranial neonatal haemorrhage. Experiences of the Referral Centre for Epilepsy of the Ministry of Health of the Republic of Croatia in treating pregnant women with epilepsy will also be presented.

Pandas Disease as a cause of epilepsy? A case report

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Background: PANDAS is an acronym for Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal infection, a rare disease that usually appears in children. It involves a subset of patients that rapidly develop obsessive compulsive disorder and/or tic disorders after an infection with group A beta-hemolytic streptococci (GABHS). The cause for this is an autoimmune reaction against a pathogen (GABHS) that shares a similar epitope with the basal ganglia, therefore affecting them and interfering (permanently) with their function. Despite the growing number of reported cases, a comprehensive review of the literature did not show any papers suggesting a link between PANDAS DISEASE and epilepsy. There is both clinical and electrophysiological evidence supporting the involvement of the *basal ganglia* in epileptic *seizures*. Basal ganglia affect activity in the frontal cortex through a series of neural projections. Materials and methods: We present the case of a previously healthy 9 year old boy who 2 weeks after a pharyngitis caused by GABHS developed a tic disorder, and a month after that developed generalized tonic-clonic seizures with an epileptogenic focus on the right frontal leads as evidenced by a video EEG. An MRI as well as a SPECT scan showed no abnormalities, but a PET scan showed increased activity in his basal ganglia. Results: the patient was left with epilepsy minimally responsive to antiepileptic drugs. Conclusion: We therefore demonstrate a connection between GABHS infection and frontal lobe epilepsy, by affecting basal ganglia functions.

Kar-mediated glutamate release facilitation at mossy fiber-ca3 synapses of the hippocampus involves calcium-calmodulin and a high calcium threshold

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Kainate-type glutamate receptors (KAR) participate in conventional neuronal transmission and processes like Long-Term Potentiation (LTP) and Long-Term Depression (LTD) that are believed to be responsible of the plastic changes that occur in the CNS during development, learning and memory and recovery after CNS lesions. The inadequate activation of KARs has detrimental effects that have been related to excitotoxicity, epilepsy and other disorders. The hippocampus is a sensitive region for epilepsy and KARs have been suggested as mediators of some of the epileptic effects of the potent neurotoxic kainate. At mossy-fiber hippocampal synapses presynaptic activation of KARs modulates glutamate release but the mechanisms involved in this modulation are not entirely known. The aim of this work was to establish the mechanisms involved in glutamate release facilitation mediated by KAR-activation at mossy fiber-CA3 synapses in mice. We used whole-cell patch-clamp recordings for this purpose. We found that activation of presynaptic KARs facilitated glutamate release via activation of adenylate cyclase (AC) by the Ca²⁺-calmodulin complex. This effect was highly-dependent on the intracellular Ca²⁺ levels and involves the entry of Ca²⁺ by L-type voltage-gated calcium channels, GluK1 containing KARs, and Ca²⁺-induced Ca²⁺ release from intracellular stores. Next step of our research is to determine whether preventing the activation of this cascade prevents some of the epileptogenic effects of kainate.

The role of epilepsy surgery treatment in quality of life of the patient with refractory epilepsy- experience from local outpatient care

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Purpose: To evaluate quality of life of the patients who underwent epilepsy surgery treatment before and after procedure in 6 months follow up in epileptologist outpatient care. Methods: The validated Czech 1.0 version of the questionnaire QOLIE-31 (health-related quality of life for adults with epilepsy) has been used to evaluate the quality of life of the patient with refractory epilepsy before and 6 months after epilepsy surgery. The questionnaire consists of 31 questions focusing on 7 sub-groups of quality of life with reachable maximum of 100 points. Descriptive statistics and a two-tailed *P*-value less than 0.05 was considered statistically significant. Results: We have prospectively examined 17 adults (8 men, 9 women) with refractory epilepsy. One man was excluded from the final analysis due to not passing the follow-up visit. Mean age while operation performed in men group was 36,25 ± 8,12 years, and in women group mean age was 36,33 ± 9,24 years. QOLIE-31 mean total score before the operation was 39,59 ± 17,80 points. After the epilepsy surgery mean total score value was 81,25 ± 21,39. Difference mean was 41,69 ± 23,05 (*p* 0.001). 15 patients improved. One patient worsened with -3,4 points difference. We also can see distinct improvement of all subgroups of quality of life except for medication category. Conclusions: We conclude epilepsy surgery as highly effective treatment of refractory epilepsy patients with significant improvement of quality of life.

Sexual dysfunction in patients with multiple sclerosis

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Background: Sexuality is an important part of health. Patients with multiple sclerosis (pwMS) may experience sexual difficulties (SD) due to multiple factors. The objective of this study was to detect possible contributing factors. Methods: This was a study conducted in tertiary care center over 10 months. SD and symptoms that interfere with sexual activity or satisfaction over the last six months were evaluated using 15-item Multiple Sclerosis Intimacy and Sexuality Questionnaire (MSISQ). Data were analysed using descriptive statistics (IBM SPSS Statistics for Windows, version 23.0(IBM Corp., Armonk, N.Y., USA)). Results: Hundred and one consecutive pwMS (75 female, 26 male; mean age 42.09 (range 19-77 years), mean Expanded Disability Status Scale (EDSS) score 3.1 (range 0.0-7.0)) participated in this study. On MSISQ 26.2% (N=16) female pwMS report inadequate lubrication, 41.7% (N=10) male pwMS difficulty with erection. 28.3% (N=23) pwMS report lack of sexual interest or desire, 19.8% (N=17) less feeling or numbness in their genitals, 32.9% (N=27) report it takes too long to orgasm or climax. In 32.6% (N=32) bladder problems, 16.3% (N=14) pain, burning or discomfort, 20.9% (N=18) tremors or shaking, and in 28.1% (N=25) muscle tightness or spasms in their arms, legs or body interfered with their sexual activity. 20.2% (N=17) report feeling less masculine or feminine due to MS. Conclusion: Multiple factors may contribute to sexual difficulties which must be considered when managing pwMS.

Regenerative therapy for cerebral palsy: transplantation of umbilical cord blood stem cells and umbilical cord mesenchymal stromal cells

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Objective: Regenerative therapy for prevention of cerebral palsy (CP) has been initiated in Japan. Hypoxic-ischemic encephalopathy (HIE) leads to CP. We already started umbilical cord (UC) blood stem cells (UCBSCs) therapy for neonatal HIE in addition to Therapeutic hypothermia (TH). We also have been preparing to start a clinical trial of UC mesenchymal stromal cells (UCMSCs) therapy for patients who did not have a sufficient effect or could not take the UC blood. **Methods:** UCBSCs was collected aseptically and prepared by using SEPAX. UC-MSCs were collected aseptically from UC and cryopreserved after culture. Infants admitted to the NICU of 6 hospitals in our research group will be eligible if they are ≥ 36 weeks' gestational age and birth weight ≥ 1800 g with HIE and meet the cooling criteria. **Results:** UCBSCs therapy for neonatal HIE in addition to TH was performed in 4 newborn patients. All of them have survived from 7 months for 1.9 years. UC-MSCs have been defined and characterized as follows; (1) abundant sources and ease of collection, storage, and transport; (2) little ethical controversy; (3) multipotency to differentiate into various cell types; and (4) low immunogenicity with significant immunosuppressive ability. **Conclusions:** Good results in combination therapy of UCBSCs and TH for newborn HIE were obtained in our 4 patients. UC-MSCs therapy will give the possibility of treatment to patients who could not take UC blood.

Testamentary capacity assessment tool: a new instrument for the evaluation of testamentary capacity in patients with dementia

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Introduction: The characterization of a person as incapable of will making, due to deficits in recall memory, is misleading because his/her intention of how and to whom he/she desires to dispose his/her assets may remain intact. Methods: We developed a short tool (TCAT –Testamentary Capacity Assessment Tool), consisting of four subtests assessing the patient's characteristics which are required for TC: memory (orientation, autobiographical memory and realistic perception of beneficiaries), existence or not of psychopathology, financial parameters (value of assets, everyday life products, bills) and intention (vignettes, theory of mind). For its validation, we examined 64 patients visiting the 2nd Department of Behavioral Neurology and Neuropsychology. The decision of the expert served as the gold standard for the evaluation of the TC. Also, the newly scale was compared to the MSSE by applying ROC analysis in both cases. Results: For the total scale by using a maximum score of 48, the best combination of sensitivity (82.6%) and specificity (100%) was obtained for a cut-off score of 32/33. Moreover, a cut-off score that can be used in order to increase the levels of sensitivity is the value 38/39: sensitivity (95.7%) and specificity (80%). The Cronbach Alpha analysis showed high levels of internal reliability for the scale ($\alpha=0.86$) and the point-biserial correlation coefficients showed high levels of criterion-related validity ($r_{bp}=0.797$, $p<0.001$). Conclusion: We believe that the TCAT is a reliable screening tool for the evaluation of TC and can be used by both the expert and the non-expert.

Fabry disease with lenticular degeneration without pulvinar sign

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Background: FD is an X-linked lysosomal storage disorder caused by a GLA gene mutation. The most frequent neuroimaging finding is non-specific T2 HSI in the periventricular white matter while the most specific MRI sign of brain involvement in FD is HSI in the bilateral pulvinar on T1WI. Case Report: A 38-year-old man visited the neurology department with a tingling sensation in both the upper and lower extremities in 2016. He had been on hemodialysis since 2009 due to end-stage renal disease (ESRD). He was diagnosed with Fabry disease (FD) via GLA gene testing [c.902GA (p.Arg301Gln) hemizygote]. The patient had been stable with regular hemodialysis. Neurologic examination showed no abnormal findings except decreased deep tendon reflexes. Brain MRI revealed high signal intensity (HSI) in the bilateral lentiform nuclei on T1-weighted imaging (T1WI), of which the core lesion was iso-intense. The core of the lesion showed low signal intensity (LSI) on T2-weighted imaging (T2WI) and diffusion-weighted imaging. There were no abnormal signal intensities in either thalamus. No other significant findings, such as cerebral atrophy or periventricular white matter changes suggesting cerebral small vessel disorders, were observed. Conclusion: In the present case, lesions were unexpectedly found in the lentiform nuclei with a similar appearance to the pulvinar signs observed in previous studies. The present case described an unusual neuroimaging finding of FD. Further observations are needed to determine whether FD should be included in the differential diagnosis of bilateral T1 hyperintensities in the lentiform nuclei.

Insufficient sleep is prevalent among migraineurs: a population-based study

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Background: The aim of this study was to evaluate the association between perceived insufficient sleep and migraine using the data of the Korean Headache-Sleep Study (KHSS). Methods: The KHSS is a nation-wide cross-sectional population-based survey regarding headache and sleep for all Korean adults aged 19 to 69 years. A difference of one hour or more between sleep need and average sleep duration indicated insufficient sleep. Results: Of 2,695 participants, 727 (27.0%) individuals were classified as having insufficient sleep. The prevalence of insufficient sleep among individuals with migraine (45.5%) was significantly higher compared to that among individuals with non-migraine headache (32.9%, $p = 0.004$) or among non-headache (20.4%, $p = 0.001$). Average sleep duration did not differ among migraine, non-migraine headache, and non-headache groups (7.3 ± 1.2 vs. 7.2 ± 1.2 vs. 7.3 ± 1.4 , $p = 0.207$). Multivariable logistic regression analyses demonstrated that migraine had an increased odds ratio (OR) for insufficient sleep after adjusting for sociodemographic variables, short sleep duration, insomnia, poor sleep quality, anxiety, and depression [OR = 2.8, 95% confidence interval (CI) = 1.9 – 4.2, $p < 0.001$]. Conclusions: The prevalence of insufficient sleep was significantly higher among migraineurs compared to that in non-migraine headache or non-headache group.

Acute interhemispheric hemorrhage manifesting solely as a headache

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Background Interhemispheric subdural hemorrhage (ISH) is a rare and distinct type of subdural hemorrhage because of their unusual location. The patient with ISH usually reported a sudden onset of painful headache with other neurological deficit. We report unusual two cases of ISH presenting headache as the sole complaint. **Case 1)** A 66-year-old man visited the outpatient clinic of neurology with a five-day history of headache. His headache was continuous, dull-pulsating in quality and located in bilateral occipitotemporal regions. The physical examinations were normal and there was no traumatic lesion. A CT scan revealed a linear high-density lesion in the posterior interhemispheric fissure, suggestive of acute ICH. Gradient Echo MRI revealed low signal intensity in the same region. **2)** An 81-year-old female visited for a gradually worsening headache for two days. The headache was bilaterally located, pulsating in quality but lasting more than 6 hours in a day. The physical examinations were normal and there was no traumatic lesion. A CT scan showed a hyperdense interhemispheric area on the right with no contrast enhancement and with a moderate mass effect. **Conclusions** The most common cause of ISH is by traumatic laceration of bridging veins between the parietooccipital cortex and the superior sagittal sinus. Even though ISH is a rare event, it should be considered among the diagnostic possibilities in elderly patients who present with headache as the sole symptom without other clinical features such as meningeal irritation signs, focal neurological deficit and alteration of consciousness.

Preventative treatment of headaches accompanied by other neurological syndromes in children and adolescents

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Discirculator headache comprises 43%, neurotic and neurosis headache 36%, liquorodinamic headache 20% of chronic headache in children and adolescents. In 66% of cases discirculator headache is accompanied by NEURO CIRCULATOR DISTONIA, in 25% by IMPAIRMENT OF ASSOCIATIVE LINKS, in 81% by AMBLYOPIA. Neurotic and neurosis headache in 30% of cases is accompanied by ENURESIS, in 20% by ASTENIC-DEPRESSIVE STATE, in 10% by NEUROTIC TICS. Liquorodinamic headache (basically in hypertension-hydrocephalic syndromes) in 30% of cases accompanied by OSCULOMOTORIC IMPAIRMENT, in 23% by PYRAMIDAL EMPAIRMENT, in 10% by AFFECTIVE-RESPIRATORY PAROXYSMS. ⁵ TREATMENT Neurotic and neurosis headache in 10% of cases runs itself when the patient is engaged in interesting for him activities. At Discirculator headache with IMPAIRMENT OF ASSOCIATIVE LINKS, we have used CITICOLINE and have observed a positive effect in 88% of cases, at Discirculator headache with NEURO CIRCULATOR DISTONIA we have used CITICOLINE+VASCULAR DRUGS and observed a positive effect in 91% cases. At Neurotic and neurosis headache with ASTENIC-DEPRESSIVE STATE we have used only ADAPTOL and observed a positive effect in 92% cases. At Neurotic and neurosis headache with ENURESIS we have used ADAPTOL+MELIPRAMIN+PANTOQAMUM, and observed a positive effect in 87% of cases. At Neurotic and neurosis headache with headache of muscle strain we have used the ADAPTOL+PANTOQAMUM+MAGNE-B6, and observed a positive effect in 55%-60% of cases. At Neurotic and neurosis headache with headache of muscle strain when we used the ADAPTO+PANTOQAMUM+MIDOKALMUM (miorelaxants) positive effects have been observed in 65% cases.

The persistence of arteriovenous malformation influences the clinical phenotype of headache secondary to non traumatic subarachnoid hemorrhage

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Background: Although the severity and suddenness of onset is the most characteristic features of headache secondary to subarachnoid hemorrhage (SAH), little is known about other headaches attributes in reference to SAH origin and its pathogenesis. Methods: The medical records of 431 consecutive non traumatic SAH patients (264 females and 167 males), ages from 19 to 91 years, presenting with headache (70.3%) and without headache (29.7%) during period of 11 years have been reviewed. Results: Among all analyzed data in reference to headaches features, although the persistence of arteriovenous malformation (AVM) was not in the association with headache occurrence in non traumatic SAH (OR 0.71 [95%CI: 0.41-1.21], p=0.213), its existence was in positive association with previous headache history (OR 1.74 [95%CI: 1.11-3.03], p=0.046), headache intensity (OR 2.24 [95%CI: 1.29-3.89], p=0.004), persistence of vomiting/nausea (OR 2.08 [95%CI: 1.13-3.83], p=0.018) and localized pain (OR 18.76 [95%CI: 9.68-36.37], p0.0001) in these patients. Conclusions: The presence of AVM is not recognized as a predictor for headache occurrence in non traumatic SAH but its existence could be associated with previous headache history, its intensity, accompanied symptoms and pain localization. *Keywords:* headache, non traumatic subarachnoid hemorrhage

Psychological mechanisms headache

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Headache is divided into three problems: - migraine - tension headache - headache not migraine or tension. Cenestopathy headache that refers to bodily hallucinations. Mechanisms of disorders: Migraine: a consequence of the impossibility of understanding to avoid some of the situations and experiences of life. This explains the swift ischemia, which extends from the occipital region to the gyrus centralis. Gyrus centralis - it is an area which is the conscious projection of the identification. Occipital area- creates a "vision". Mental inability to connect "Seen", that is unacceptable to interpret the established way of identity with the identity - leads to the attack of disconnection of the possibility of by ischemia distance between them. Tension headache. Two options: The lack of resources in the process of thinking - for example, do not have enough information; Incorrect use of inappropriate information- imputing meaning. Cenestopathy headache: a violation of the psychological treatment of mental pain. Subspecies - phantom headache. Often of other somatization when psychic pain experienced through physical symptoms, and his head felt as something burdensome. Characteristically for hypertension.

Correlation of a hypocretin-2 receptor polymorphism with cluster headache susceptibility and a serotonergic 5-hydroxytryptamine receptor polymorphism with triptan treatment response

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Cluster headache (CH) is a primary neurovascular headache with an increased hereditary risk. The less common A allele of the CH associated *HCRTR2* gene polymorphism rs2653349, seems to reduce disease susceptibility. The *GNB3* gene polymorphism rs5443 was associated with positive triptan treatment response. Carriers of the mutated T allele are more likely to respond positively to triptans compared to C:C homozygotes. DNA from buccal swabs of 1464 non related individuals was collected and analysed. Gene distribution for the polymorphism rs2653349 was G:G=77.8%,G:A=20.3% and A:A=1.9%. The frequency of wild-type G allele was 92.3%. The frequencies for rs5443 polymorphism were C:C=44,8%,C:T=41.9% and T:T=13.3%.The frequency of wild-type C allele was 70.0%. The odds ratio of male vs. female volunteers for rs2653349 exhibited no statistically significant difference, but for rs5443 polymorphism a statistically significant difference ($p=0,0292$) between the genders could be demonstrated. Comparison of study population polymorphism frequencies vs. other populations showed that rs2653349 A allele appeared only 7.7% while in global and in European population the frequency was 12,1% and 18,4% respectively. Further, we observed that male homozygotes for the protective mutant allele are 2-fold more than female. Results indicate that investigated Greek population has great similarity to the European population regarding rs5443 allele and genotype distribution. Based on our results we could assume that the pathophysiology of CH is affected by multiple factors, however, the genotyping analysis of polymorphisms may play a significant role in susceptibility and treatment of CH suffering patients.

Parinaud syndrome and mri findings

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Introduction: We examined if neurophthalmological findings in patients with Parinaud syndrome (PS) differ between patients with intrinsic (intraaxial) and extrinsic (caused by pineal gland tumors) brainstem lesions. Methods: Medical records of patients with PS were retrospectively reviewed. Results: Twenty six patients with PS were identified. Eight patients had extrinsic brainstem lesions with hydrocephalus. Two patients had hydrocephalus due to aqueduct stenosis and ependymoma of the fourth ventricle, respectively. Sixteen patients suffered from intrinsic brainstem damage (ten tumors, five vascular and one traumatic lesion), seven were associated with hydrocephalus. The most frequent finding was convergence – retraction nystagmus (85%), followed by light-near dissociation of pupil reaction (80%), upgaze limitation (46%) and eyelid retraction (27%). The ophthalmological findings did not differ between patients with extrinsic or intrinsic brainstem lesions. Patients with low or moderate brainstem lesions and hydrocephalus had more clinical findings than patients with the same degree of brainstem involvement without hydrocephalus ($p= 0.03$ and $p=0.04$). The resolution rate of the ophthalmological findings did not differ between individual subgroups. A complete resolution was achieved in 8% patients, partial in 25% and 67% of patients remained unchanged. Conclusions: The routine MRI techniques do not allow conclusions about the ophthalmological findings in patients with PS. The presence of hydrocephalus is an important factor influencing the clinical findings in intrinsic lesions. The prognosis of PS is less favorable than generally reported.

Sensory nerve fibres are involved in amyotrophic lateral sclerosis

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Introduction: It is accepted that motor neurons invariably degenerate but sensory nerves are generally considered to be intact in ALS. However, in the last two decades, supportive arguments on sensory involvement in ALS came from both neurophysiological evaluations and pathological studies. In this study we assessed sensory involvement in ALS patients. Methods: Nerve conduction studies (NCS), somatosensory evoked potentials (SSEP), laser evoked potentials (LEP), and quantitative sensory testing (QST-at least 2 abnormal tests) were performed in 16 definite and 2 probable ALS patients based on Awaji criteria and 31 controls. In addition, skin biopsies were evaluated in ALS patients using quantification of intraepidermal nerve fiber density (IENFD). Results: The percentages of abnormal neurological examinations, NCS, SSEP, LEP, QST, and skin biopsies were 38.8%, 72.2%, 56.6%, 72.2%, 11.1% and 16.6%, respectively. Conclusions: Our study confirmed that sensory fibers are involved in ALS. The pattern of sensory involvement in ALS (myelinated sensory fibers are affected more than unmyelinated ones) is opposite to what we usually see in distal symmetric sensory polyneuropathies.

Clinical application of autologous mesenchymal stem cells in amyotrophic lateral sclerosis: Yes or no? The Greek experience

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Objective: The evaluation of safety and clinical effectiveness of the transplantation of autologous mesenchymal stem cells (MSCs) in greek patients with amyotrophic lateral sclerosis (ALS) and discussion of the results according to the scientific references. Methods: Forty patients (Group A) with definite ALS were enrolled in the study. Bone marrow was collected from the posterior iliac crest and MSCs were expanded at the laboratory of the Hellenic Cord Blood Bank (HCBB) of the Biomedical Research Foundation of the Academy of Athens (BRFAA). The cells suspended in 2 ml of autologous CSF were transplanted intrathecally. A second group of patients with ALS (Group B) without transplantation was also enrolled in the study. The clinical progress of the disease was evaluated by the ALSFRS-R scale. An evaluation of the clinical profile of the two groups with the ALSFRS-R before and after the transplantation has been done for a long period with a follow up of 4 years. Results: A significant slowing down of the decline of the disease after transplantation has been ascertained during these 4 years. Conclusion: Our results demonstrate that the injection of MSCs intrathecally to ALS patients is safe well tolerated and without adverse events.

Association of *tbc1d1* gene variants with sporadic amyotrophic lateral sclerosis in Greek patients

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Amyotrophic lateral sclerosis (ALS) is one of the most common forms of motor neuron disease. ALS is a neurodegenerative disorder that affects the upper and lower motor neurons in the motor cortex, brain stem, and spinal cord and leads to death within 3-5 years. Approximately 90% of the ALS patients suffer from sporadic ALS, having both an environmental etiology and a strong genetic component. Today, there is no effective treatment or diagnostic means for ALS patients. We have previously identified novel genomic loci to be associated with sporadic ALS in sporadic ALS patients of Greek origin. Here, we have performed whole-genome sequencing of 10 ALS patients and 7 healthy (non-ALS) individuals of Hellenic origin, using the DNA nanoballs proprietary approach of Complete Genomics Inc (110x sequencing depth). Following extensive data analysis, we identified 174 genomic variants that were present in all 10 ALS patients but none of the 7 non-ALS ethnically matched controls. Replication of genotyping in 27 sporadic ALS patients and 50 ethnically matched control individuals showed that *TBC1D1* genomic variants are positively associated with the disease phenotype ($p=0.017$). *TBC1D1* has been identified as a regulator of insulin-dependent glucose transport and variants in the *TBC1D1* gene were linked to obesity. This is the first study that reveals an association between the *TBC1D1* gene and ALS pathobiology. Nevertheless, due to the small sample size, this should only be considered a pilot study and replication in a larger population cohort is needed to confirm this finding.

Hypermetabolism in als: complication or part of pathogenesis?

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Hypermetabolism is one of not motor-related signs of ALS. Hypermetabolism in ALS has not been fully elucidated, but its signs could be detected before first motor symptoms of ALS. The aim of our study was to investigate the prevalence and severity of hypermetabolism in early stage ALS patients of the Russian population and try to clarify its correlation with neurodegeneration. The study concerned 40 ALS patients and 20 patients of the control group. Hypermetabolism was valued via questionnaires, anthropometric and biochemical dates (blood levels of albumin, lipoproteins and zinc-alpha 2-glycoprotein, ZAG, as an adipokine). The rate of neurodegeneration was estimated by clinical and anamneses' dates and levels of marker (phosphorylated heavy chains of neurofilaments, pNfH). Concentrations of markers were measured in CSF and blood of patients by ELISA. According to our investigation hypermetabolism was diagnosed about in half of cases of early stage ALS. Levels of pNfH were significantly different in ALS and control groups: 350,2 pg/ml [150; 500] и 65,2 pg/ml [48; 148] correspondingly. Levels of ZAG were not significantly different: 48,9 mcg/ml [40,7; 60] in ALS and 45,6 mcg/ml [42,6; 49,9] mcg/ml in control group. Also a slight positive correlation of pNfH and ZAG in CSF was detected. Prevalence of hypermetabolism in early stage ALS patients of Russian population is high and comparable with previously published dates. Results of biochemical study show that hypermetabolism is involved in pathogenesis of ALS already in an early stage of the disease, but further studies are needed to determine its exact role.

Glioblastoma following treatment with interferon beta-1a for relapsing-remitting multiple sclerosis

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Introduction: Glioblastoma is an uncommon and aggressive primary brain tumor with an incidence of 3 per 100,000 annually. Several types of brain tumors have been described in association with multiple sclerosis (MS) such as astrocytoma, oligodendroglioma and glioblastoma. Possible predisposing factors to this co-existence include a subclinical immunosuppressive state and the activation of autoimmune mechanisms in effort to induce remyelination. We report a 45 year-old woman diagnosed with glioblastoma within 10 years of induction of interferon beta-1a therapy for relapsing- remitting MS. To our knowledge this is the first report of a potential association between interferon and glioblastoma development. Conclusion: MS patients have an increased risk for brain and genitourinary tumors. Diagnostic procedures relating to the differentiation between pseudotumoral MS lesions and gliomas are imperative. The role of immunosuppressive treatment of MS in carcinogenesis remains a matter of debate.

Dawson fingers point to dielectrophoretic force in the etiology of multiple sclerosis disease

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Thus far, Dawson fingers (DFs), which are periventricular, ovoid and oriented perpendicularly to the ventricular surface, have been assumed to be the lesions of multiple sclerosis. These lesions have been characterised as mechanical damage resulting from the differences in blood pressure along the Virchow-Robin spaces, or the spaces around the veins. After a Magnetic Resonance Imaging (MRI) scan, formations similar to DFs can be seen in the shape of a wedge in some regions of the brain: in particular, in the ependymal surfaces, the vertex of the blood vessels, and some areas around the posterior and anterior horns. These DF-like formations in the brain cannot be explained by mechanical damage. The purpose of this study is to determine the main formation mechanism of these DF-like formations in the brain. The main cause of DFs is secondary electromagnetic radiation from the collecting veins, which are perpendicular to the ventricular surface. In this context, the antenna model approach to DFs is crucial; in fact, it is the tenth new clue of the Canbay hypotheses on the etiology of multiple sclerosis (MS). Using the Canbay hypotheses, the potential places for the initiation of these plaque formations can be estimated.

Pulmonary toxicity due to alemtizumab` s infusion. diagnostic and treating dilemmas

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Introduction: Alemtizumab is a novel monoclonal antibody indicative for active relapsing remitting multiple sclerosis. Alemtizumab targets CD52 protein of mature B and T lymphocytes, leading to their depletion. The most notable adverse events are immune mediated conditions like idiopathic thrombocytopenic purpura, thyroid disorders or nephropathies and also infusion-associated reactions. Case description: A 21 year old woman showed at the fourth day of alemtizumab infusion acute chest pain, cough and shortness of breath with no fever. The x-ray detected lung consolidation at both sides and the following computer tomography (CT) confirmed the lower lobar consolidations with focal ground-glass opacity and numerous small opacities through lungs. The differential diagnosis included pneumonia, infection of pneumocystis carinii and drug-induced interstitial lung disease (DILD). Alemtizumab was withdrawn and antibiotic treatment was initiated. The next day the patient was improved as did the imaging exams, so antibiotics discontinued and she got only supportive care and corticosteroids. Ten days later the new CT was normal and symptoms had totally been resolved. Discussion: Alemtizumab could cause pulmonary toxicity and immune inflammation to the lungs maybe due to drug specific antibodies or T cells. But how easy is to diagnose DILD in a patient under immunosuppression treatment excluding other etiologies considering the lack of consensus for a diagnostic approach in patients with DLID? How should been determined the prognosis? Because alemtizumab is an immunosuppression drug with increased risk to cause infections have the antibiotics a place in the DILD` s treatment? Is there a risk for relapse in future rechallenge with alemtizumab.

Coexistence of multiple sclerosis and systemic sclerosis. Diagnostic and treatment considerations

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Background: Coexistence of autoimmune diseases and multiple sclerosis (MS) has been reported. Wherever if not there is a genetic association between them has to be clarified. MS is rarely reported in association with systemic sclerosis (SSc). Herein we report on a case of with long-lasting SSc which presented with sensory disturbances and finally came out with the diagnosis of MS. Case report: A 43-year-old woman was admitted with a 20-days history of sensory disturbances. These started as numbness on the feet and progressively came up to the low thoracic region bilaterally and symmetrical, reflecting transverse myelitis. On brain and spinal cord MRI demonstrated dissemination of lesions in space and time, thus full-filling the revised 2010 Mc Donald criteria for MS. The diagnosis of coexistence of MS was made after excluding alternative diagnosis. Among the FDA approved immunomodulatory first line treatments glatiramer acetate was preferred due to less known link to autoimmune diseases. Discussion: Despite MS is been frequently reported in association with other autoimmune diseases is rarely described in coexistence with systemic sclerosis. Systemic sclerosis is characterized by immune dysregulation which includes also interferon inducible genes. As is known from the literature some MS cases treated with interferon beta (INF-beta) subsequently developed systemic sclerosis. Maybe INF-beta precipitates immune-mediated abnormalities. Conclusion: INF-beta as treatment for MS coexistent with SSc should be avoided as it could result in significant deterioration of SSc.

Multiple sclerosis and celiac disease, case report.

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1. Background Multiple sclerosis (MS) is an immune mediated inflammatory disease of the central nervous system (CNS). The diagnosis was based on clinical, laboratory and radiological data according to Mc Donald's criteria. Based on etiology MS seems to be associated with other autoimmune diseases. A correlation between gluten intake and incidence of MS had been reported and a relationship of anti gliadin antibodies and MS was debated. The research studies found an increased prevalence of celiac disease (~11.1%) with MS. Case Report: We report the case of a 30 years old female, who was consulted in our clinic for the first time 15 years ago (2001) presented with: spastic paraparesis and paresthesias in upper and lower extremities. MS diagnosis was done. She had relapsing remitting episodes with the same symptoms, evaluated with EDSS 3.0 Kurtzke and was treated with intravenous methylprednisolone. The b1-Interferon is applied for three years. Episodic generalized tonic clonic seizures happened during the first years. During the last year the patient complains gastrointestinal disorders such as constipation, diarrhea and extremely weight loss. We suggested Celiac disease and autoimmune thyroiditis screening for autoantibodies and gastrointestinal endoscopy. The biopsy supports the celiac disease diagnosis. The patient was given gluten-free diet for celiac disease and she has a weight gain and gastrointestinal disorders improvement. 3. Conclusion: MS is known to be associated with other autoimmune diseases. Some studies revealed the association between MS and CD. MS patients with gastroenterological complaints should be tested for gluten sensitivity and other gastrointestinal autoimmune disorder.

Improvements in patient-reported treatment satisfaction with teriflunomide: results from the phase 4 teri-pro study

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INTRODUCTION: Teriflunomide is a once-daily oral immunomodulator for relapsing-remitting MS. The global, phase 4 study, Teri-PRO (NCT01895335), examined patient-reported outcomes, and the effectiveness, safety, and tolerability of teriflunomide treatment in routine clinical practice. **METHODS:** Patients with relapsing forms of MS received teriflunomide 7 mg or 14 mg for 48 weeks, per local labeling. The primary outcome was Global Satisfaction at Week (W) 48, measured using the Treatment Satisfaction Questionnaire for Medication (TSQM, v1.4). TSQM scores were measured at baseline (for patients switching from prior disease-modifying therapy [DMT]), and at W4 and W48/end of treatment (all patients). **RESULTS:** For 1000 treated patients, mean (SD) age was 47.1 (11.0) years; mean time since first MS symptoms was 13.2 (9.5) years. Mean (95% CI) TSQM scores were similar between W4 and W48: Global Satisfaction 72.3 (71.0,73.6)/68.2 (66.4,70.0); Side Effects 88.4 (87.2,89.7)/84.1 (82.5,85.7); Convenience 92.3 (91.6,93.1)/90.4 (89.4,91.3); Effectiveness 67.1 (65.8,68.4)/66.3 (64.7,67.9). In 594 patients who switched from a prior DMT within 6 months, improvements in all TSQM subscales were observed from baseline to W4, and maintained at W48 (*P* **CONCLUSIONS:** Results from Teri-PRO showed high levels of treatment satisfaction with teriflunomide at W4 and W48 across all TSQM domains. Patients switching to teriflunomide from other DMTs reported a sizeable increase in treatment satisfaction at W48 vs baseline. Previously presented atECTRIMS 2016. Study supported by Sanofi Genzyme.

Efficacy of Alemtuzumab Is Durable Over 6 Years in Patients With Active Relapsing-Remitting Multiple Sclerosis and an Inadequate Response to Prior Therapy in the Absence of Continuous Treatment (CARE-MS II)

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BACKGROUND: Patients with active RRMS and inadequate response to prior therapy (≥ 1 relapse after ≥ 6 months of treatment) had improved outcomes with alemtuzumab versus SC IFNB-1a over 2 years (CARE-MS II; NCT00548405). An extension (NCT00930553) demonstrated durable efficacy through 5 years in the absence of continuous treatment. **GOAL:** Evaluate 6-year efficacy and safety of alemtuzumab in CARE-MS II patients. **METHODS:** Patients received 2 courses of alemtuzumab 12 mg (baseline: 5 days; 12 months later: 3 days) in CARE-MS II with as-needed alemtuzumab retreatment for relapse/MRI activity, or another DMT per investigator discretion, in the extension. **Assessments:** ARR; freedom from 6-month CDW (≥ 1 -point EDSS increase [≥ 1.5 -point if baseline EDSS=0]); 6-month CDI (≥ 1 -point EDSS decrease [baseline score ≥ 2.0]); NEDA; AEs. **RESULTS:** Through 6 years, 344/393 (88%) patients remained on study. ARR remained low (Year 6: 0.15). 72% of patients were free from 6-month CDW; 43% achieved 6-month CDI. Mean EDSS increase from baseline was 0.10 (Years 0–6); 77% had improved or stable EDSS at Year 6. Most patients achieved annual NEDA (Year 6: 60%). 50% received no additional treatment after 2 initial courses of alemtuzumab. AEs decreased over time. Thyroid AEs peaked at Year 3 then declined. Infusion-associated reactions decreased with additional treatment courses. Serious AE rates, including infections, were low. **CONCLUSION:** Efficacy was maintained over 6 years with 50% of patients receiving no additional treatment after 2 initial alemtuzumab courses. Based on these findings, alemtuzumab may provide a unique treatment approach with durable efficacy in the absence of continuous treatment.

Brain volume loss correlates with long-term disability worsening in patients with ms: siena analysis of temso mri data

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Introduction: In TEMSO (NCT00134563), SIENA (structural image evaluation using normalization of atrophy) analysis determined that, vs placebo, teriflunomide significantly reduced brain volume loss (BVL), which was strongly correlated with disability worsening. Subgroup analyses showed that teriflunomide significantly slowed BVL vs placebo independently of disability worsening over 2 years. Here, we explore BVL and long-term disability worsening in TEMSO and its extension (NCT00803049). **Methods:** Blinded SIENA analysis of patient scans (n=969) determined BVL in Year 1 and Year 2. Percentage brain volume changes (PBVC) from baseline to Year 2 were categorized into quartiles (Q1–Q4) to evaluate probability of 12- and 24-week confirmed disability worsening (CDW) over 5 years in the extension. Probability of worsening was derived from Kaplan–Meier estimates. Quartiles were compared using a Cox proportional hazards model (covariates: PBVC categories, baseline Expanded Disability Status Scale strata, and region). **Results:** Patients with scans in Q1 (n=177; greatest BVL from baseline to Year 2) had a significantly higher risk of 12- and 24-week CDW after 5 years than those in Q4 (n=178; lowest BVL from baseline to Year 2): Q1 vs Q4 hazard ratios, 0.611 (95% CI: 0.432, 0.865; $P=0.0055$) and 0.566 (95% CI: 0.386, 0.830; $P=0.0036$) for 12- and 24-week CDW after 5 years, respectively. **Conclusions:** Results provide further evidence of the association between BVL and later disability worsening. Greater rates of BVL over 2 years are predictive of longer-term disability worsening at 5 years in the TEMSO extension. Study supported by Sanofi Genzyme. Previously presented at ECTRIMS 2016.

"The treatment with Natalizumab of relapsing remitting ms in children: Yes or no? The Hellenic experience"

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Objective: To elucidate the efficacy and safety of Natalizumab in pediatric Multiple Sclerosis in all children from our cohort who were placed on Natalizumab per clinician's judgment. Methods: Clinical history and outcomes in 11 children with aggressive relapsing-remitting MS (2 boys, 9 girls), age of MS onset 13.3 years [range 10-16 years] were reviewed in our database. The first disease-modifying treatments for nine children were either IFN- β or Glatiramer Acetate. These children transitioned to Natalizumab after a year due to lack of clinical or radiological response. The 10th and 11th cases, were immediately started on Natalizumab due to a very aggressive disease presentation. Patients received between 5-40 monthly treatment infusions and were followed for between one and eight years. Results: With regards to treatment efficacy, the median annualized relapse rate (ARR) decreased from three to zero and disability measured through the EDSS scale decreased from a range between two and six to one after a year. There were no active lesions on MRI a year after treatment initiation. With regards to safety, there was no evidence of adverse events or hypersensitivity reactions. Conclusion: Multiple Sclerosis is not an adults privilege. Natalizumab is an effective and safe treatment for pediatric MS that is either of an aggressive nature or does not respond to common first line disease modifying therapies. Longer follow-up periods will allow better prediction of long-term safety and efficacy on degenerative disease features. There is less danger for PML in children. References: Chitnis T. Neurotherapeutics 2013 Jan;10(1):89-96 Waldman A., Brenda Banwell et al Lancet Neurol. 2014, 13 :936-48 Arnal-Gracia C. et al Eur. J. of Paed. Neurology 2013; 17:50-54 Ghezzi A. et al BMC Neurology 2015;15:174

Identifying neuropathic back and leg pain in patients with multiple sclerosis

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Introduction and aim: The aim of this study was to investigate the prevalence of nociceptive or neuropathic low back pain (LBP) amongst patients with multiple sclerosis (MS). Methods: The study was conducted on 85 MS patients with LBP with or without leg pain. PainDETECT neuropathic pain screening questionnaire (PDQ) was used to identify likely pain mechanisms. Based on the PDQ scores, participants were classified into three groups: a neuropathic pain group, a nociceptive pain group, and an unclear pain group. Hospital Anxiety and Depression Scale was used to measure depression and anxiety. The degree of disability was based on the Expanded Disability Status Scale (EDSS), whereas the severity of pain was measured using a visual analogue scale. Results: A total of 31.8% of participants (n=27) reported nociceptive pain, 32.9% (n=28) unclear, and 35.3% (n=30) neuropathic pain. Among them, patients with clear nociceptive and neuropathic LBP were selected. Patients in the neuropathic pain group had significantly higher pain intensity (t=3.569, p=0.001) and higher prevalence of anxiety (t=1.417, p=0.5). There were no statistically significant between-group differences according to age (t =1.557, p=0.125), sex (t=1.51, p=0.5), EDSS score (t=0.009, p=0.993), MS course (t = 1.041 p = 0.303), disease duration (t=1.250, p=0.217) and prevalence of depression (t=0.29, p=0.5). Conclusion: Based on screening test results, MS patients suffer from either neuropathic or nociceptive LBP, which has implications for the choice of treatment strategy. Key words: Multiple sclerosis, low back pain, PainDETECT questionnaire.

Healthy children and disease stable mothers with multiple sclerosis

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Background: Multiple sclerosis (MS) affects fertile women who ask for a safe pregnancy. **Goals:** To find the most efficient strategy to shorten the preconception period and the proper time to return to disease modifying treatment (DMT). **Methods:** Our strategy used in 38 women with MS receiving DMT and planning their pregnancy resulted in the birth of 34 healthy children (also a pair of twins) and a minimal risk for disease worsening. Patients were psychologically supported and educated to plan pregnancy, after stopping DMT, birth control pills and other contraceptive methods used 3 months prior to conception, in order to have a regulate menstrual cycle. They performed gynecological clinical and ultrasound examination to exclude local problems, tests to exclude local or general infections, specific hormonal tests and anti Mullerian Hormone test. All treatable problems were solved before stopping DMT. Sperm grams of their partners were performed. Intercourse occurred in the ovulation days (3-4 times), after 3 days of male abstinence. No toxics or drugs were used. **Results:** DMT safely discontinued had a high percent of rapid pregnancies and healthy children. They returned to the same DMT no later than 8 weeks after delivery, initial breastfeeding being possible and no/minimal neurostatus worsening was observed. Patients were permanently monitored by the neurologist and obstetrician-gynecologist. **Conclusions:** The patient should remain uncovered by DMT for as little time as possible and this goal can be reached by planning and performing specific tests and treatments for the couple before stopping DMT and returning to DMT treatment.

Clinicians' perceptions of how current practice meets multiple sclerosis patient needs: results from a qualitative survey

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Background: The MS in the 21st Century initiative is led by a steering group (SG) of international multiple sclerosis (MS) specialists and patient advocates with the current focus to improve communication and education between physicians and people with MS. Objective: To understand the views of the MS clinical community on unmet patient needs, with emphasis on patient support, treatment decisions, and the concept of disease progression. Method: Across two workshops, the SG of MS specialists and patient advocates developed an electronic survey piloted at the European Committee for Treatment and Research Congress in MS (ECTRIMS), 2016. Multiple answers were solicited in response to six questions. Results: All respondents (n=57) reported at least one challenge at diagnosis, including lack of time to explain progression (33%) and offer emotional support (39%). Approaches to discussing progression varied: 32% rely on patient-led discussion and 39% use analogies to explain difficult concepts; 46% would like more resources to aid discussion. Patient participation in treatment decisions (67%) varied; 21% reported lack of time or resources to accommodate involvement, 56% explain treatment side effects and benefits and 23% would like more 'risk versus benefit' written/online information. There was no consensus on the most important factor for patients making treatment decisions. Conclusion: Clinicians recognised a lack of time and resources, particularly at diagnosis; there was not enough time to offer the emotional support patients needed. However, variation in clinicians' perceptions of patient's priorities, and the disparity in discussing disease progression, suggests a need for understanding the patient perspective.

Alemtuzumab Durably Slows Brain Volume Loss Over 6 Years in the Absence of Continuous Treatment in Patients With Active RRMS Who Were Treatment-Naive (CARE-MS I) or Had an Inadequate Response to Prior Therapy (CARE-MS II)

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BACKGROUND: Alemtuzumab significantly slowed brain volume loss (BVL) over 2 years versus SC IFNB-1a in active RRMS patients who were treatment-naive (CARE-MS I; NCT00530348) or had inadequate response (≥ 1 relapse) to prior therapy (CARE-MS II; NCT00548405). Efficacy was durable through 5 years in an extension (NCT00930553) in the absence of continuous treatment. **OBJECTIVE:** Evaluate effect of alemtuzumab on BVL over 6 years. **METHODS:** Patients received 2 courses of alemtuzumab 12 mg (baseline: 5 days; 12 months later: 3 days), with as-needed alemtuzumab retreatment for relapse or MRI activity, or another DMT per investigator discretion, in the extension. BVL was derived by relative change in brain parenchymal fraction. **RESULTS:** Through 6 years, 325/349 (93%) CARE-MS I and 344/393 (88%) CARE-MS II patients remained on study. Alemtuzumab slowed median yearly BVL over 2 years, maintaining low BVL in Years 3–6 in CARE-MS I (Year 1: -0.59% , Year 2: -0.25% , Year 3: -0.19% , Year 4: -0.14% , Year 5: -0.20% , Year 6: -0.17%) and CARE-MS II (Year 1: -0.48% , Year 2: -0.22% , Year 3: -0.10% , Year 4: -0.19% , Year 5: -0.07% , Year 6: -0.10%) patients. 63% (CARE-MS I) and 50% (CARE-MS II) of patients received no additional alemtuzumab and no other DMT after 2 initial alemtuzumab courses. **CONCLUSIONS:** Slowing of BVL with alemtuzumab was maintained over 6 years in RRMS patients, with median annual BVL $\leq 0.2\%$ in Years 3–6 in both studies. Based on these findings, alemtuzumab may provide a unique treatment approach with durable efficacy in the absence of continuous treatment.

Diverse role of macrophages in experimental autoimmune encephalomyelitis: a controversy

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Organ specific central nervous system (CNS) autoimmune diseases including experimental autoimmune encephalomyelitis (EAE), a model of human multiple sclerosis, has been known to be caused by autoreactive T cells and bystander macrophages. The inflammatory lesions are characterized by the infiltration of T cells and monocyte originated macrophages, followed by reactive microgliosis and astrogliosis. There is a general agreement that classically activated M1 macrophages play an important role in the initiation of CNS tissue damages. Recently alternatively activated M2 macrophages has been found in the EAE lesions with concurrent remission of paralysis in Lewis rats. The source of M2 macrophages in rat EAE lesions remains controversial whether they are originated from either monocytes or microglial cells, or both. As for the phenotypic switch of macrophage or microglia, in vivo EAE study shows that phenotypic switch occur in Iba-1 positive macrophages (monocyte and/or microglia) because either inducible nitric oxide synthase⁺(M1 marker), arginase-1⁺ (M2 marker), or both –positive macrophages were found in EAE lesions. It is postulated that spontaneous recovery of EAE paralysis in rats is closely related with the relative prevalence of M2 milieu of inflammatory lesions, in which M2 macrophages secrete tissue protective molecules including heat shock protein and TGF beta. The control of macrophage phenotypes would be an alternative therapeutic strategy in organ specific autoimmune diseases. This research was supported by the Basic Science Research Program of the National Research Foundation of Korea (NRF), funded by the Ministry of Education (Grant number: NRF-2014R1A1A2055965).

Lower urinary tract symptoms in patients with multiple sclerosis

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Background: Patients with multiple sclerosis (pwMS) commonly report overactive bladder (OAB) symptoms of urinary urgency, incontinence and frequency, as well as the inability to void to completion. The aim of this study was to evaluate lower urinary tract symptoms (LUTS) and their impact on quality of life (QoL) in people with multiple sclerosis (pwMS). Design/Methods: This was a study conducted in tertiary care center over 10 months. LUTS and related QoL were evaluated using International Consultation on Incontinence Questionnaires (ICIQ): ICIQ-OAB, ICIQ-UI (urinary incontinence) and ICIQLUTS-QoL. Data were analysed and interpreted using descriptive statistics (IBM SPSS Statistics for Windows, version 23.0 (IBM Corp., Armonk, N.Y., USA)). Results: Hundred and one consecutive pwMS (75 female, 26 male, mean age 42.09 (range 19-77 years), mean Expanded Disability Status Scale (EDSS) score 3.1 (range 0.0-7.0)) participated in this study. On ICIQ-OAB 35.6% (N=36) pwMS report increased daytime frequency, and 23.8% (N=24) borderline symptoms (7-8 times a day). 82% (N=82) report nocturia, 90.9% (N=90) urgency, with urge UI present in 72.4% (N=71). On ICIQ-LUTSQoL 91% (N=91) report feeling drowsy and sleepy during the day due to LUTS. 87% (N=87) had to plan to use a public washroom. In 56.7% (N=55) LUTS caused an issue with their partner of spouse. Conclusion: Lower urinary tract symptoms may be present in pwMS and may have an influence QoL. This must be considered when managing pwMS.

Genetic anticipation - true or false?

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Background: The phenomenon in which a genetic disease has an earlier onset and a more aggressive evolution with each succeeding generation was controversial. However, anticipation has now been proven to occur in a large number of important genetic disorders, including myotonic dystrophies. Case report: A 41-year-old man has had locomotor difficulty since he was 18 years old. Later, he noticed difficulties in vowel pronunciation and recently, a slowed relaxation following a normal muscle contraction. Neurological examination reveal hypertonic hands and feet muscle, atrophy in the masseter, temporalis, sternocleidomastoid muscles and distal legs muscles, distal motor deficit in wrist extension, walking without aid, early balding, triangular facies. Genetic tests revealed on a chromosome (allele) 5 ± 1 CTG repeats and on the other chromosome (allele) more than 300 CTG repeats. The pattern is characteristic for DM (muscular dystrophy) type 1 (Steinert's disease). His parents were apparently healthy, but his father has early baldness and cataracts, without any complaints. The patient has two girls, 8 and 15 years old. The older one has had signs and symptoms of DM1 disease for 4-5 years and EMG and genetic test confirmed it, with an increased number (over 300) of the CTG trinucleotide repeat in DMPK gene. Conclusion: This case report represents an example of a real genetic anticipation. Grandfather, father and daughter associate mild, classic and congenital phenotypes, respectively. Thus, genetic counseling and prenatal testing is mandatory for pregnancies at increased risk when the diagnosis of DM1 has been confirmed in an affected family member.

Alteration of the Motor Unit Potential (MUP) in Myasthenia Gravis (MG)

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Aim: The MUP in the MG are controversial and based on insufficient number of patients investigated. The series of investigations were carried out, in which detailed analysis of the MUP parameters in the MG patients was made and their alterations in respect to the muscles' functional state were studied. **Methods:** Electromyographic (EMG) investigations were carried out in 400 muscles of 104 patients with serious forms of MG. The abductor muscle of the fifth finger and other various muscles were investigated. The data obtained assessed the students t-criteria. **Results:** The MUPs of the MG patients are characterized with decreased mean duration of the potential and pronounced drop of the amplitude. High value of the polyphasic and spontaneous activity is not revealed. Manifestation of the spontaneous activity MG is concerned with denervation alterations, confirmed by: practical absence of the fibrillation potentials and the positive spiky waves in the patients with reversible damages of the neuromuscular transmission; higher manifestation of spontaneous activity in muscles, where an adequate dose of Neostigmine does not elevate the mean duration of the MUPs. **Conclusion:** All the above-mentioned indicate high diagnostic value of recording of the MUPs and spontaneous activity during MG. Both the Neostigmine test and the EMG investigations provide for the assessment of the depth of neuromuscular transmission infringement as well as for reversibility of the process in a separate muscle. Advantage of the method for investigation of MUPs and spontaneous activity of the motor units in the MG diagnostics has been determined in testing of any kind of muscle.

A practical approach to acute flaccid paraplegia: a case series

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Introduction: Acute flaccid paraplegia is a clinical occurrence of extreme importance, due to the dramatic presentation, the severity of the underlying disorder, and the generally poor prognosis that follows such a condition. Materials and methods: During 2014, we dealt with eleven cases of acute non-traumatic paraplegia, in our neurological facility. A thorough electrophysiological, serological and imaging study has been performed in all cases. An ad hoc therapy was implemented as well, within the best standard of care as of actual. The majority (8/11) were warranted a diagnosis of polyradiculoneuritis. Discussion: Among etiological factors, the traumatic events are of particular interest, with the treating clinical dealing with a severely ill patient, following fall from height, motor vehicle collisions, and direct shocks applied over the vertebral column. The non-traumatic list is more numerous; however the severity of the acute paraplegia is not necessarily of a lesser degree. Viral infections, autoimmune disorders, and ischemic events involving feeding spinal arteries have been imputed. Chemical and medications injected intrathecally during procedures or accidentally can produce acute flaccid paraplegia. In spite of the poor prognosis, different therapeutic options have been proposed and applied. Conclusions: Surgery interventions are often necessary when trauma is present, with high dose glucocorticoids treatment preceding the intervention, aiming to decrease edema-related compression over the spinal cord. Immunoglobulins and plasmapheresis are logical and helpful options when a polyradiculoneuritis produces such a clinical picture. With the casuistics suggesting that even intra or extra axial tumors invading the spinal canal are able to imitate this event, the role of decompression seems by far of a particular significance.

Effect of flickering of led light on cognitive event-related potentials**Ki-Young Jung², J. Sunwoo¹**¹*Neurology, Soonchunhyang University Seoul Hospital, South Korea*²*Neurology, Seoul National University College of Medicine, South Korea*

Purpose: It has been well established that light condition affected the brain function including cognitive processes. However, exact mechanisms of these effects have not been fully understood. Development of light-emitting diode (LED) allowed us to control light conditions in more detail. In this study, we examined the effects of LED light flicker on working memory by using event-related potential (ERP). **Materials and Methods:** Twenty-six healthy subjects participated in this study (mean age, 30.4 years; men 66.7%). Sixty-channel scalp EEG was recorded under two different conditions: control flicker (40%) light and flickerless (1%) light. Color temperature and brightness were set as 4,000 K and 500 lux in both conditions. Each light condition consisted of four blocks: 3 min in a dark condition (resting block), 4 min in one of the light condition (EEG block), 15min with working memory task (ERP block), and 3 min in a relaxed state (relaxation block). Data were epoched from 200ms prestimulus and 1,200ms poststimulus. We analyzed ERP component, time-frequency, functional connectivity data by using Matlab (MathWorks, USA). **Results:** Among ERP component, P2 component (from 160 ms to 200 ms) tended to increase in parietal and occipital areas under flickerless condition ($p = 0.038$ and 0.021 , respectively). However, P3 component did not differ between two light conditions. Time-frequency analysis revealed no significant difference in all frequency bands. Regarding functional connectivity, flickerless light increased theta-band connectivity in both item 2 and 3 conditions ($F_{1,18} = 8.633$, $p = 0.009$). In addition, theta-band connectivity was significantly correlated with refreshing and comfort scores ($p = 0.012$ and 0.040 , respectively). **Conclusions:** This ERP study demonstrated that flickerless light enhanced the theta-band functional connectivity during the working memory process compared to control flicker light.

Antidepressants for post-traumatic brain injury depression: a meta-analysis of randomized controlled trials

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Introduction: Patients with traumatic brain injuries (TBIs) suffer from depression at a frequency varying between 16-60%. Considering that brain injuries afflict mainly young individuals, the need for effective treatment is imperative. **Methods:** We performed a systematic review and meta-analysis of randomized controlled trials (RCTs) from January 1990 until November 2016 comparing the efficacy of antidepressants with placebo in the treatment of post-TBI depression. We searched MEDLINE, SCOPUS and the CENTRAL Register of Controlled Trials. **Results:** Four placebo-controlled RCTs investigating the Selective Serotonin Reuptake Inhibitors (SSRIs) citalopram and sertraline complied with the eligibility criteria of our search. Even though at the end of the follow-up period the rate of non-responders was found to be lower in the treatment groups compared to placebo (OR=0.42, 95%CI=0.15-1.17), this difference was not statistically significant (p=0.10). In the subgroup analysis of the studies that reported mean Hamilton Depression Scale for Depression between treatment and control patients on both the baseline and endpoint evaluations, the pooled mean difference was reduced from 2.11 (95%CI=-1.25-5.46) to -2.36 (95%CI=-5.59-0.87) in favor of the treatment group. Despite this reduction, statistical significance was marginally unattainable (p=0.06). No evidence of heterogeneity or publication bias were observed among the included studies. **Conclusion:** Citalopram and sertraline seem to be effective in treating patients with post-TBI depression. Due to the lack of high quality data on this devastating problem of public health, there is an urge for appropriately designed and adequately powered RCTs extending to other newer antidepressants.

Prevalence in depression after stroke

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Aim: To determine the prevalence of depression after stroke; To determine differences in prevalence of depression between the sexes and between age. **Methodology:** 186 (83F&103M) patients admitted at University Clinic of Neurology in UHC "Mother Teresa", Tirana, Albania; diagnosed for ischemic stroke were assessed initially, by examination and interview. This patients are followed from 4 to 12 months by the psicosocial staff of our center in their houses. back inventory of used to measure the degree of depression clinical interviews .For each patient was prepared a folder to compare changes in time as a result of intervention of psychosocial. **Results:** The prevalence of depressive illness 4 months after stroke in 186 patients was 28%,major depression and 12% minor depression. There were small differences between the sexes and small diferenc from the ages . With a non-hierarchic approach to diagnosis of those with depression, 43% of men and 31% of women had an associated anxiety disorder. 12% of male and 15% of female patients interviewed had evidence of depression at the time of stroke. 12 months after stroke 42% of the men were still depressed, as were 26% of the woman and 22% joungest patients were still depressed and 37% older. **Conclusion:** The prevalence of depression after stroke was comparable with that reported from other studies. They have small differences between sexes was revealed and small differences for ages.

The `face of the giant panda` in a purely neuropsychiatric presentation of Wilson`s disease

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38 year old male referred by his GP with 6 months history of progressive ataxia, changes in his demeanour, and tremor. The neurological examination revealed fine bilateral hand and leg tremor, side to side head tremor, finger nose hypermetry, dysdiadochokinesis and choreiform tongue movements. On the Addenbrooke`s cognitive test he showed marked deficits in memory and visual-spatial skills. Ophthalmic examination revealed Kayser–Fleischer rings. The brain MRI depicted extensive symmetrical high signal changes involving the corticospinal tracks at the level of the basal ganglia extending to the brainstem. Furthermore diffuse signal abnormalities were noted, affecting the cerebellar white matter, the midbrain, pons and thalami. As seen on the MRI the red nucleus and substantia nigra produce lower signal compared to the surrounding tissue forming `the face of the Panda`, as seen in less than 3% of the neuropsychiatric presentations. A challenging diagnosis as the patient presented in his late thirties without any hepatic involvement. It is highly didactic as it teaches the importance of broad differential and the need for early recognition of possible reversible causes. Prompt involvement of the Neuro-Radiology MDT and Discussion in Grand rounds is always beneficial towards achieving correct diagnosis.

Deep brain stimulation in parkinson`s disease and x-linked dystonia-impact on quality of life: a descriptive study

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Deep brain stimulation has been recently introduced in the Philippines as a procedure to control or alleviate symptoms of movement disorders such as X-linked Dystonia and Parkinson's Disease. In our institution, a total of 11 patients (X-linked Dystonia and Parkinson's disease) have been granted and are being followed up for their neurostimulators. This study describes the quality of life of these patients after deep brain stimulation in terms of physical and psychosocial domains. It was limited to the patients who have active neurostimulator. Sickness index profile (SIP), a 136 item questionnaire, was used. Seven patients consented to be part of the study, 2 of whom are PD patients and 5 are XDP patients. The mean sickness index score obtained was 38.85 (28%) with more impairment of psychosocial functions. Adapting a validated cut - off score (SIP score of 33 +/- 13) from Volkmann et al, our results translates a poor quality of life among these patients.

Impact of pain and pain subtypes on the quality of life of patients with Parkinson's disease

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Background: Pain is a frequent and troublesome non-motor symptom in Parkinson's disease (PD) and has a negative impact on QoL of PD patients. The aim of this study is to investigate the relative impact of pain or a specific pain subtype on the QoL of the PD patients. **Methods:** We included 161 PD patients. Pain was assessed using the patients' descriptions, a structured interview, a detailed neurologic examination, and the visual analogue scale (VAS). QoL was assessed using the 39-item Parkinson's disease questionnaire (PDQ-39). **Results:** One hundred and twenty (74.5%) PD patients had chronic pain. Musculoskeletal pain was the most prevalent type, followed by radicular/neuropathic, dystonic, and central. PD patients with pain, regardless of pain subtype, had a higher PDQ-39 score than PD patients without pain. Multivariate regression analysis showed that the high score of PDQ-39 was related to PD onset age, UPDRS-II score, Beck depression inventory (BDI), and VAS score. **Conclusion:** Pain along with depression, poor ADL, and younger PD onset age is associated with poor QoL and all subtypes of pain affect QoL of PD patients.

Cigarette smoking, coffee intake and alcohol consumption preceding Parkinson`s disease: a case–control study

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Background: Although genetic factors play a role in the development of Parkinson's disease (PD), the lack of a clear genetic underpinning has led to investigation of the role of environmental factors in the etiology of PD. **Objective:** A case–control study was performed in Belgrade in order to investigate the association between PD and smoking, coffee and alcohol consumption. **Methods:** 110 new PD cases and 220 hospital controls were interviewed. Cases and controls were matched by sex, age and place of residence. Conditional univariate and multivariate logistic regression methods were used. **Results:** With PD were associated, independently from each other, current smoking [odds ratio (OR) = 0.44; 95% confidence interval (CI) = 0.23–0.82], alcohol consumption (OR = 4.78; 95% CI = 2.67–8.55) and coffee consumption (OR = 2.54; 95% CI = 1.36–4.75). In ever smokers the risk for PD significantly decreased with the increasing number of cigarettes smoked and with increasing duration of smoking. The risk for PD significantly increased with the increasing quantity of alcohol consumption. PD risk was significantly higher in subjects whose average daily consumption of coffee was 1 and 2–3 cups, and it was lower (but not significantly) in those whose daily coffee consumption was 4+ cups. The results of multivariate analyses did not substantially change after adjustment on family history positive on PD. **Conclusion:** The findings of this study support the hypotheses of inverse association of smoking with PD, but an inverse association with coffee was not confirmed. PD was found to be positively associated with increased alcohol consumption.

The cholesterol oxidation derivative 27 hydroxycholesterol regulates α -synuclein transcription-implications in synucleinopathies

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Accumulation of α -synuclein protein is a common hallmark of a group of brain disorders collectively known as synucleinopathies. These disorders include Parkinson's disease, dementia with Lewy bodies, multiple system atrophy and Alzheimer's disease. The causes of synucleinopathies are likely multi-factorial with several factors including genetic susceptibility and environmental agents, potentially participating in the pathogenesis of these diseases. 27-hydroxycholesterol (27-OHC) is an oxysterol produced from oxidation of cholesterol by the mitochondrial enzyme CYP 27A1. Cholesterol oxidation to 27-OHC is accelerated not only by diets rich in cholesterol but also by oxidative stress and aging. When formed in excess, 27-OHC has the ability to cross lipophilic membranes of the blood brain barrier and migrate into the brain where it can increase α -synuclein levels through over-activation of its cognate receptor, liver X receptor (LXR). We have incubated human neuroblastoma (SHSY5Y) cells, mouse dopaminergic neurons differentiated from embryonic stem cells, and human dopaminergic neurons differentiated from human normal dopaminergic neuronal precursor cells with 27-OHC and examined the effects of increased 27-OHC on the expression levels of α -synuclein. Our results show that 27-OHC dose-dependently increases the transcription of α -synuclein through modulation of LXR in the three different cell types. Identification of the oxysterol 27-OHC and the LXR as the underlying cellular mechanisms by which 27-OHC increases α -synuclein levels may help in designing therapeutic agents that can prevent, reverse, or stop the over-production of α -synuclein and ultimately may protect against *synucleinopathies*.

Optic nerve and macula morphology in patients with Parkinson's disease using optical coherence tomography

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Purpose: To investigate optic nerve and macular morphology in patients with Parkinson's disease (PD) using spectral-domain optical coherence tomography (SD-OCT). **Methods:** 25 participants with PD (19-males and 6-females; mean age 60.79; SD \pm 9.24) and 25 gender-, age-, ethnicity- and refraction-matched healthy controls were enrolled in a prospective, cross-sectional, observational study. High-resolution SD OCT (Copernicus, 3 μ m resolution) was used to acquire scans centred on the optic disc and fovea. **Main outcome measures:** Optic nerve head parameters (disc/cup diameters/areas, cup/rim volumes, cup depth, cup/disc ratio; peripapillary retinal nerve fibre layer (ppRNFL) thickness, retinal thickness and thickness of individual retinal layers. **Results:** Our study showed significant ppRNFL thinning in PD patients in all quadrants ($p < 0.05$) associated with a shallower optic cup ($p = 0.03$) as compared to healthy controls. Foveal remodelling with retinal thinning (nasal and temporal segments in both annuli; and superior segment in outer annulus; $p < 0.05$), foveal pit widening ($p = 0.05$), central OPL thickening ($p < 0.001$) and nasal RPE thinning ($p < 0.001$) was also found in PD. Changes were more pronounced in advanced stages of PD and with longer diseases duration. **Conclusions:** Optic nerve changes in PD are likely to be caused by primary neurodegeneration and are different to ON changes described in glaucoma. Central retinal thinning, pit widening, central OPL thickening and RPE thinning indicate that remodelling of the fovea occurs. Specific changes of the fovea and thinning of individual retinal layers, correlating with disease severity and duration indicate that ON and retinal changes have potential to be used as biomarkers for PD.

Non-motor symptoms of parkinson`s disease: gender and age features and their dependence on the stage of the disease

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In recent years increasing attention is paid to non-motor symptoms (NMS) of Parkinson`s disease (PD) as their manifestations are significantly different in patients of various age and gender groups. The goal of our research was to investigate the expression of PD NMS, depending on the age and gender of patients and stage of the disease. The study involved 255 patients with PD, 56.9% of which were men, 43.1% were women. The course of the disease, including NMS in daily life, was evaluated according to unified PD rating scale. The stage of the disease was determined by Hoehn and Yahr scale. We found growth rate of PD NMS in a group of women. In senile age patients this index was significantly increased compared with groups of young ($p=0.036$) and average age women ($p=0.016$). Also direct correlations were observed between age ($r=0,33$; $p=0.021$), stage of the disease ($r=0,37$; $p=0.028$) and severity of NMS. Index of PD NMS in a group of men was also increased. But in senile age men this index significantly reduced compared to a group of women of the same age ($p=0.038$). Also directly proportional dependence was observed between stage of the disease and its NMS ($r=0,32$; $p=0.023$). The data of our research indicate that NMS of PD are the most pronounced in senile age women, and their direct dependence with the stage of PD according to the Hoehn and Yahr scale was observed.

Ameliorating effects of new neurotensin analogue and vasoactive intestinal peptide in parkinson's disease model

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Parkinson's disease (PD) results in progressive loss of dopamine neurons and leads to movement disorders such as tremor at rest, slowness of voluntary movements, rigidity, postural instability. Using rat experimental model of PD via unilateral injection into striatum (target coordinates AP = +0.2; LR = -3.0; H = -5.6 according to stereotaxic atlas) of 6-hydroxydopamine we aimed to study: i) effects of new neurotensin analogue (NT2) on rat motor performance and brain activity; ii) effects of vasoactive intestinal peptide on the levels of glutathione reductase activity and lipid peroxidation in rat brain. Our results demonstrated gradual improvement in the motor performance of NT2-treated animals as compared to control PD-rats treated with saline. At the same time cortical EEG showed differences in spectral composition and patterns above the lesioned areas and their hemispheric counterparts in the PD-rats treated with NT2 as compared to saline treated PD-animals. Our experiments also demonstrated that vasoactive intestinal peptide decreased the activity of enzyme glutathione reductase and inhibited lipid peroxidation in the experimental model of Parkinson's disease counteracting in such way against membrane damage and ameliorating the cell viability. In conclusion the beneficial effects of vasoactive intestinal peptide and new neurotensin analogue outlined in the present investigations may represent a new therapeutic option for control of some Parkinson's disease disorders.

Dopamine transporter image in Niemen-pick disease type c

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Niemann-Pick disease type C (NP-C) is a rare autosomal recessively inherited lysosomal storage disorder characterized by progressive neurological symptoms and various degrees of visceral involvement. The patient was a 24-yr-old male presented with psychosis, abnormal posturing, and gait disturbance. His birth and development had been unremarkable. At the age of 18, He started to develop delusion and abnormal posturing on both hands. At 21, He had to be hospitalized in department of psychiatry because of troublesome psychosis such as visual and auditory hallucinations, aggressive and impulsive behavior. He also developed gait disturbance and cognitive impairment around that time. Despite of symptomatic treatment, all symptoms were gradually aggravated, so at the age of 24, he became completely dependent on caregivers and wheelchair bound. Family history revealed that his younger sister had similar symptoms. On neurologic examination, He showed generalized dystonia that is prominent in both upper limbs, severe ataxic gait, VSGP and severe dysarthria. Brain Magnetic resonance image (MRI) showed no definite signal change, but mild atrophy of posterior part of brain was seen and ¹⁸F-FP-CIT positron emission tomography (PET) scan showed mildly decreased uptake in right caudate and anterior putamen. NPC1 gene sequencing revealed a compound heterozygote mutation which was already known as a genetic cause of NP-C, one in exon 9 (c.1552CT [R518W]) and one in exon 18 (c.2780CT [A927V]). Filipin staining test of cultured fibroblasts from skin, which is another key diagnostic test for NP-C, was done and the result was positive. There has been no systematic study in NP-C using ¹⁸F-FP-CIT scan that demonstrate presynaptic dopaminergic neuronal loss. Our case had decreased dopaminergic uptake in ¹⁸F-FP-CIT scan, but the pattern was much differ from parkinson's disease, in which deficit is predominantly in dorsal, posterior putamen.

5'-Chloro-5'-Deoxy-(±)-Enba, A Potent And Selective Adenosine A₁ Receptor Agonist, Inhibits The Harmaline-Induced Tremor And Zif-268 Mrna Expression In Rats.

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Harmaline is commonly used to model essential tremor (ET) in animals. The main cause of harmaline-induced tremor is abnormal activation of the olivo-cerebellar glutamatergic climbing fibers, elevation of glutamate release and increase in complex spike discharges of Purkinje cells of the cerebellar cortex. Adenosine A₁ receptors are present in all the brain structures associated with the harmaline-induced tremor (inferior olive, cerebellum, thalamus and cerebral cortex). Furthermore, an intrathalamic infusion of an A₁ agonist decreased the harmaline tremor in mice.

The aim of this study was to examine the role of A₁ receptors in the harmaline-induced tremor in rats using 5'-chloro-5'-deoxy-(±)-ENBA (ENBA), a potent and selective A₁ agonist. Harmaline-induced tremor (15 mg/kg *ip*) was measured automatically in Force Plate Actimeters. The zif-268 mRNA expression was additionally analyzed by *in situ* hybridization in several brain structures. ENBA (0.05-0.5 mg/kg *ip*) dose-dependently reduced the harmaline-induced tremor and the effect of ENBA (0.1 mg/kg *ip*) was reversed by DPCPX, a selective A₁ antagonist (1 mg/kg *ip*). Harmaline increased the zif-268 mRNA expression in the inferior olive, cerebellar cortex, ventroanterior/ventrolateral thalamic nuclei and motor cortex. ENBA reversed those increases in all the above structures and DPCPX reduced the ENBA effect only in the motor cortex. The present study suggests that adenosine A₁ receptors may be a potential target for the treatment of ET. *Supported by statutory funds and National Science Center grant no. 2013/11/B/NZ4/04565. B. Kosmowska is a holder of scholarship from the KNOW funds sponsored by Ministry of Science and Higher Education, Poland.*

Painful leg and moving ankle syndrome

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Background: Painful leg and moving toe syndrome is characterized by pain in the feet or lower limbs and spontaneous movement of the toes. The variants of this syndrome include phenotypes affecting the upper limbs, with symptoms such as painful hands and moving fingers. We present a case of chronic leg pain associated with involuntary ankle movements. **Case Report:** A 43-year-old woman presented with a 3-month history of involuntary movements of the left ankle, which appeared insidiously and an 18-month history of left leg pain and paresthesia. The involuntary movements of the left ankle had a roving pattern with some jerky components. No spontaneous toe movements were observed. The pain did not respond to various analgesics. Lumbar spinal magnetic resonance imaging revealed left-sided disc protrusions at the L3-4 and L4-5 levels. Nerve conduction studies showed left peroneal and lateral femoral cutaneous neuropathy. The ankle movements did not respond to clonazepam, baclofen or anti-dopaminergic agents. The ankle movements resolved when the pain subsided spontaneously 6 months later. **Comments:** Involuntary ankle movements can be associated with moving toe syndrome. However, to the best of our knowledge, isolated movement of the ankle in association with proximal leg pain has not been described previously. The present case illustrated a rare type of involuntary distal movement associated with neuropathic leg pain.

Role of kinins receptor b2 in therapy of Parkinson's disease in animal model

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Parkinson's disease (PD) a neurodegenerative disorder, is characterized by the loss of dopaminergic neurons in the substantia nigra and its projections into the striatum causing various motor deficits. Nowadays, treatment mostly relies on L-DOPA administration; however, effects produced by this drug are limited and cause diverse side effects. Treatment of PD is initiated at progressed stages of PD, since symptoms only become evident after a loss of at least 50 % of dopaminergic neurons in the substantia nigra accompanied by a drastic reduction of dopamine content in the striatum. The slow and progressive death of dopaminergic neurons let to suggest therapeutic strategies aiming at protection of the remaining ones against apoptosis and stimulation of neurogenesis for replacement of lost neurons. In view of that, the exploration of neuroprotective, self-renewal of stem cells inducing and neuroregenerative properties of bradykinin may help to substitute lost dopaminergic neurons in addition to enhance the survival of reminiscent neurons. The bioactive peptide bradykinin obtained from cleavage of precursor kininogens activates the kinin-B2 receptor functioning in induction of inflammation and vasodilatation. Recent evidence suggests that bradykinin participates in kidney and cardiovascular development and neuronal differentiation. Here we show that kinin-B2 receptors and the participation of bradykinin in neuroregeneration in a rat model of PD induced 6-OH-dopamine injection. Bradykinin injection following establishment of PD symptoms resulted in improvements in the lesioned areas as studied by tyrosine hydroxylase immunostaining and motor functions.

Wolfram syndrome presenting with upbeat nystagmus

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Wolfram syndrome (WFS) is a rare autosomal recessive genetic disorder characterized by diabetes insipidus, diabetes mellitus, optic atrophy and deafness. Imaging studies revealed atrophy of brainstem and cerebellum in WFS but its clinical significance remained unclear. A 18-year-old woman visited to our hospital for anosmia which had developed two years before the admission. She had been diagnosed with diabetes mellitus at the age of 3 and bilateral optic atrophies at the age of 11. On admission, the patient was totally blind and video nystagmography revealed upbeat nystagmus in central gaze both with or without fixation. MRI of the brain demonstrated diffuse atrophy of brainstem and cerebellum. Diagnostic exome sequencing test revealed two distinct variants (c.1232_1233delCT; p.Ser411Cysfs*131 and c.2168TC; p.Leu723Pro). WFS is associated with smaller intracranial volume with specific abnormalities in the brainstem and cerebellum even at the earliest stage of clinical symptoms but there is a variable degree of mismatching between clinical and radiologic findings in brainstem and cerebellum of WFS patients. Pendular nystagmus and gaze-evoked nystagmus have been described as the corresponding neurological deficit. Upbeat nystagmus is commonly localized to the caudal medulla, more rostral brainstem lesions with interruption of the ventral tegmental tract, or brachium conjunctivum in the rostral pons and medulla. Although the specific neural substrate for the abnormality is not clear, it is possible that brainstem and cerebellar abnormality in WFS present with upbeat nystagmus in this case.

Documentation of a Striatal Glutathione Deficit *In Vivo* in Parkinson's Disease Directly Implicates Oxidative Stress in Disorder Pathophysiology

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Background: *Postmortem* studies of Parkinson's disease (PD) brain have consistently reported deficits of nigrostriatal glutathione (GSH) – the primary living tissue antioxidant– of up to 40% compared to normal brain, strongly implicating oxidative stress in the pathophysiology of PD. However, direct evidence corroborating a striatal GSH deficit in PD brain *in vivo* is currently lacking. This study assessed whether there is a GSH deficit in living PD brain by directly measuring cortical levels of the antioxidant *in vivo* with MRS. **Methods:** For this pilot study, 22 patients diagnosed with idiopathic PD per the United Kingdom Parkinson's Disease Society Brain Bank criteria, and 27 medically healthy volunteers (HV) were recruited. *In vivo* spectra of GSH were measured in 15 min with proton MRS on a 3T GE MRI system from voxels of interest in the left striatum and the occipital cortex (OCC). **Results:** In the striatum, the region of primary interest, GSH in PD patients was 15% lower ($p=0.04$) than in the HV group. In the OCC, a region not directly implicated in PD, there was a trend-level lower GSH ($p=0.08$) in PD patients than in the HV group. **Conclusion:** This study has obtained what may be the first *in vivo* evidence of a nigrostriatal GSH deficit in PD compared to healthy subjects, a finding that corroborates *postmortem* PD brain results that have consistently shown striatal GSH deficits and are the basis for a pathophysiological model of PD that places oxidative stress centrally in disorder pathogenesis.

Rbd and other sleep disorders in a cohort of p.a53t snca mutation carriers

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REM sleep behavior disorder (RBD), defined as REM sleep without atonia (RWA) plus either dream enactment behavior, sleep related injuries, potentially injurious or disruptive behaviors, documented by medical history, or polysomnography (PSG), may occur in association with neurodegenerative diseases, mainly α -synucleinopathies. In idiopathic Parkinson's Disease (PD) RBD may precede the motor manifestations of the disease. There is a general question whether PD due to defined genetic causes, transmitted through Mendelian inheritance, is similar to idiopathic PD. In this regard, it is especially interesting to assess whether RBD and other sleep abnormalities occur in carriers of the p.A53T alpha-synuclein gene (SNCA) mutation, the prototypical genetic synucleinopathy. Such a systematic study has not been performed previously. We have accordingly assessed 10 p.A53T carriers with PSG, Epworth Sleepiness Scale, RBD Screening Questionnaire (RBDSQ), UPDRSIII and MOCA. Three of the p.A53T carriers were asymptomatic, had no evidence of RBD in PSG and scored ≤ 5 in RBDSQ. All 7 symptomatic p.A53T carriers had evidence of sleep disorder in PSG. Three were diagnosed with RBD in PSG, however 2 of them were treated with antidepressants and only 1 of them scored 5 in RBDSQ. In three others, PSG showed RWA, but only 1 of them scored 5 in RBDSQ. The last one was diagnosed with PLM in PSG, was not treated with drugs and scored 5 in RBDSQ. We conclude that RBD or RWA occur in the majority of PD p.A53T manifesting carriers, possibly at a higher percentage compared to idiopathic PD.

Is it possible to develop a preclinical diagnosis of parkinson`s disease, basing on a search for biomarkers? Is there an alternative approach?

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Motor symptoms first appear in Parkinson`s disease (PD) years after beginning of degradation of the nigrostriatal dopaminergic system at loss of threshold amount of dopamine (DA) in the striatum (70%), which explains low efficiency of treatment. Therefore, the development of preclinical diagnosis of PD is a high priority. Considering the systemic pathogenesis of PD, current methodology is based mainly on finding biomarkers, such as non-motor clinical symptoms and changes in body fluids (blood, CSF) and blood cells. A number of weak points makes this methodology doubtful: (i) there is no guarantee that biomarkers found in body fluids of patients at clinical stage are also characteristic of patients at preclinical stage; (ii) considering that individual biomarkers (non-motor symptoms, changes in body fluids) are semi-specific, it is necessary to use a battery of biomarkers; (iii) the diagnostic procedure should be too expensive for mass examinations. This methodology can be improved by additional searching biomarkers in animals at modeling preclinical PD, although it will always remain nonspecific. Importantly, the alternative approach. the provocative, or challenge test can be successfully used for specific preclinical diagnosis of chronic internal diseases. Provocative test is used to specifically and reversibly enhance latent failure of a defective organ to the threshold level, thereby causing a short-term appearance of specific symptoms. We have proven the validity of this methodology for the development of preclinical diagnosis of PD by systemic administration of a reversible inhibitor of dopamine synthesis to 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine-treated mice at the presymptomatic stage of parkinsonism. Principal publication: Khakimova GR, Kozina EA, Kucheryanu VG, Ugrumov MV, Reversible pharmacological induction of motor symptoms in MPTP-treated mice at the presymptomatic stage of parkinsonism: Potential use for early diagnosis of Parkinson`s disease. *Mol Neurobiol.* 2016 May 19. [Epub ahead of print].

Dopamine synthesis by non-dopaminergic neurons in the striatum at Parkinsonism – a paradoxical reality

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Parkinson's disease (PD) is developed for a long time at preclinical (asymptomatic) stage, despite the loss up to 70% dopamine in the striatum that is due to neuroplasticity. Neuroplasticity in the striatum is manifested in stimulation of functional activity of survived dopaminergic neurons and an increase of sensitivity of target neurons to dopamine. In addition to the dopaminergic axons, ascending from the substantia nigra, striatum contains intrinsic non-dopaminergic neurons expressing one of the enzymes of dopamine synthesis – tyrosine hydroxylase (TH) or aromatic L-amino acid decarboxylase (AADC). Among mammals, the number of these monoenzymatic neurons is especially large in primates, and it increases significantly in PD. When modeling PD at preclinical and clinical stages in mice with 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), we have shown for the first time that: (i) monoenzymatic neurons expressing complementary enzymes of dopamine synthesis produce this neurotransmitter in cooperation in MPTP-treated mice, but not in intact animals, (ii) the proportion of dopamine synthesis by monoenzymatic neurons in the striatum increases at the progression of neurodegeneration. Cooperative synthesis of DA was proved using the original model of inhibition of DA synthesis in striatal slices by blocking transport of L-DOPA, produced in monoenzymatic TH neurons, to AADC neurons by means of L-leucine, a competitive inhibitor of the membrane transporter of large neutral amino acids, and L-DOPA. Thus, the cooperative synthesis of dopamine in the striatum under dopaminergic deafferentation is an up-regulated compensatory reaction, which is among the principal mechanisms of neuroplasticity in PD. Principal publications: M. Ugrumov (2009) Non-dopaminergic neurons partly expressing dopaminergic phenotype: Distribution in the brain, development and functional significance. *J Chemical Neuroanat.*, 38, 241-256. Kozina, A. Kim, A. Kurina, M.Ugrumov. (2017) Cooperative synthesis of dopamine by non-dopaminergic neurons as a compensatory mechanism in the striatum of mice with MPTP-induced Parkinsonism. *Neurobiology of Disease* 98, 108-121.

Case and control study: higher prevalence of neuropathy in patients with secondary hyperparathyroidism

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Background: Diabetic neuropathy is frequent in the population with diabetic nephropathy (DN); however, there is no information about whether secondary hyperparathyroidism increases its incidence. The purpose of this study was to determine, through symptoms and signs, if there was neuropathy increased frequency in a group of patients with DN with hyperparathyroidism, compared to a control group. **Methods:** This is a case and control prospective observational study that was composed of patients with DN having 60 pg/ml serum parathormone (PTH) values, named control group (CG). The Hyperparathyroidism group (HG) was formed by patients with DN and ≥ 60 pg/ml PTH values. The variables were: body-mass index, diabetes evolution time, and presence of diabetic neuropathy (Michigan Test). The minimum calculated sample consisted of 60 cases in each group. The variables on scale were compared to the Student's t-test and the percentages to Chi2. **Results:** There were 60 cases in each group: 35 (58.3%) men in CG versus 33 (55.0%) in HG ($P = 0.713$). The age for CG was 67 ± 11.0 years vs 72 ± 11 for HG ($P = 0.009$). The glomerular filtration in CG was 53.82 ± 25.13 , and in HG, it was 35.34 ± 18.43 ml/min/1.73 m² ($P = 0.001$). The PTH in CG was 38.02 ± 15.32 pg/ml, and in HG, it was 119.07 ± 84.33 pg/ml ($P = 0.001$). The neuropathy through symptoms in CG was 28.3 % while in HG, it was 36.6% ($P = 0.330$). The neuropathy through signs in CG was 38.3%, and in HG, it was 83.3% ($P = 0.001$). The odds ratio for HG to present neuropathy through signs was 8.044 (IC95% 3.42 – 18.92). **Conclusion:** In the subjects suffering from diabetic nephropathy who were studied, neuropathy had more prevalence in the group affected with secondary hyperparathyroidism. Therefore, statistical association was evident between secondary hyperthyroidism and the presence of diabetic neuropathy in patients with DN. **Key words:** Secondary hyperparathyroidism, complications, diabetic neuropathy, renal failure, adult.

Characteristics of the restless leg syndrome in patients with diabetic polyneuropathy

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The clinical picture of Restless Legs Syndrome (RLS) is diverse with the wide range of common symptoms of diabetic polyneuropathy (DPN), such as unpleasant feelings, pain, burning sensation, cramps, crawling that might disappear during the movement of the legs. The aim of the study was to examine the efficacy of pramipexole in patients with DPN resistant to standard therapy. The study involved 84 patients with type 2 diabetes mellitus complicated with DPN. In 25 (29.76%) patients, (main diagnostic criteria used), RLS was found. There were 2 groups: I group - 13 patients received gabapentin with dose titration up to 2.4g per day; II - 12 patients received pramipexole 0.750 mg once a day. Patients were interviewed on a quality of life at RLS scale before and 30 days after the treatment. Social function was $9,51 \pm 0,05$ points; after the treatment, the average score in the first group was $18,21 \pm 0,12$ points ($p < 0,05$). In the second group, the patients proved a more positive trend, which was $21,51 \pm 0,11$ points ($p < 0,05$). Sleep violation bothered all patients ($15,21 \pm 0,14$ points). In the first group, it was $19,03 \pm 0,17$ points ($p < 0,05$) after the treatment, whereas the patients of the second group indicated a significant improvement ($26,15 \pm 0,18$) ($p < 0,05$). Conclusions. In patients who were resistant to treatment with gabapentin, RLS should be suspected, because of the similarity of symptoms with DPN and pramipexole therapy must be assigned.

A case of acute ophthalmoplegia without ataxia associated with anti gd1b igg antibody

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It is known that acute ophthalmoplegia without ataxia was reported to be mostly elevated anti-GQ1b antibody titer. It is very rare that anti-GQ1b antibody is negative but another ganglioside antibody-positive such as anti-GM1b, GD1b antibodies. In previous cases, high anti GM1 antibody alone or GM1, GD1a and GD1b antibodies in acute ophthalmoplegia without ataxia were reported. We reported case that only elevated anti GD1b antibody titer in acute ophthalmoplegia without ataxia. A 53-year-old male presented ptosis of the left eye with progression of the ptosis in both eyes 2 weeks ago admission to our department of neurology. On the next day of admission, he presented bilateral ophthalmoplegia. Pupil light reflex, deep tendon reflex were normal and ataxia were absent. Other neurologic examination were unremarkable. Brain MRI showed no ischemic or hemorrhagic lesions and nerve conduction test and anti acetylcholine receptor antibody test were normal. In cerebrospinal fluid analysis, protein was elevated (82.0 mg / dl) and other index were unremarkable. The oligoclonal band was negative and thyroid function tests was normal. Anti-GD1b IgG antibody titer was increased mildly to 38.62 (normal value 30) but other anti ganglioside antibodies were normal ranges. He was given intravenous methylprednisolone 1g/day for 7days and oral prednisolone tapered. After 1 month, ophthalmoplegia and ptosis were undergoing some improvement without ataxia or areflexia. We experienced rare case of acute ophthalmoplegia associated with isolated elevated anti GD1b antibody titer. Further researches for correlation of ophthalmoplegia with antiganglioside antibody other than anti GQ1b antibody.

A tricky progressive weakness

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A 63 years old man, presented with 10 days story of lower limbs weakness, he reported a previous pneumonia treated with antibiotics. Symptoms have been worsened and forced him to use a stick before admission. Neurological examination showed pure motor paresis of lower limbs, with proximal strength graded 3/5 while spared distal movements, conserved flexion plantar reflexes and brisk tendon reflexes. He presented a marked increase of CPK (14799), GOT (741) and GPT (266). Electrophysiological studies showed normal amplitude of motor and sensor nerve action potential and distal conduction velocity, EMG showed a reduced recruitment in ileopsoas and deltoid muscles but no myositic signs. Suspecting a miopathy, he was treated with intravenous infusion of 1 mg metilprednisolone for 5 days. On hospital day 3, the paresis became worse: consisting in inability to lift legs from the bed and areflexia. His CSF examination revealed 130 protein and cell count of 2. Viral-bacterial tests and serological tests for self-directed and paraneoplastic antibodies were negative. Further ENG study showed prolonged F-wave latencies, poor F-wave repeatability and prolonged distal latencies, consistent with demyelination of nerve roots; normal recruitment muscle pattern, no fibrillation. He was treated with immunoglobulins 0.4 mg/kg for 5 days. During the first 5 days of therapy the weakness was spreading to the arms: proximal inability to keep arms lifted, conserved grasp strength; areflexia of upper limbs. Later he started a slow recovery, and 15 days after therapy neurological examination showed no strength deficit in upper limbs and ability to lift lower limbs up for few seconds. This is an example of GBS associated with myopathy; few cases are reported in literature with such increase in CPK. This case should teach to think about GBS even if the clinical pattern is uncommon, in case of prolonged F waves and albumino-citological dissociation.

Tabes dorsalis showing abnormal somatosensory evoked potential with normal spine mri finding

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Background: Tabes dorsalis is a late manifestation of untreated syphilis that is characterized by sensory ataxia, lancinating pains, and urinary incontinence. Pathologically, there is degeneration of the posterior roots and column of the spinal cord. Case report: A 43-year-old man presented with progressive difficulty in walking and tingling paresthesia in the lower limbs for 5 months. On examination he showed hypesthesia on below T12 level, sensory ataxia, generalized hyporeflexic deep tendon reflex and Argyll Robertson pupil. Serum FTA-ABS was positive and serum RPR was reactive (1:64). Both CSF FTA-ABS and CSF VDRL were positive. CSF examination also manifested WBC count $90/\text{mm}^3$ (lymphocyte 93%), protein 72mg/dl, glucose 53mg/dl. HIV ELISA was negative and serum vitamin B12 level was within normal limit. Genetic study for spinocerebellar atrophy was negative and nerve conduction study was also negative. Magnetic resonance imaging (MRI) of the whole spine showed no definite intramedullary abnormal findings. MRI of the brain also showed normal result. Median somatosensory evoked potential (SEP) was normal, but posterior tibial SEP revealed increased lumbar to cortical central conduction time, suggesting a spinal defect mainly below the cervical region. He was treated with aqueous crystalline penicillin G, 3 million units intravenously every 4 hours for 14 days, which relieved his ataxic gait. Follow up posterior tibial SEP after 6 months documented shortening of lumbar to cortical central conduction time. Conclusion: This is the first case report of tabes dorsalis with normal spine MRI finding but abnormal SEP result, correlating with patient's symptom.

Computer mouse drawing and motor pattern development

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The idea of the study was based on observations collected during daily-life of our family. We analyzed two sources of data. The first one was the set of sketches made by a 7-year-old girl during her natural drawing activity, and the other one was experience of one of the authors in drawing with the use of a traditional computer mouse. Observations of motor task execution after changing the tool for a new one were analyzed in the context of data from two lectures regarding human motor pattern development that were delivered by other authors. Changing the drawing tool for a new and more difficult resulted in new ideas and topics, as well as in increased creation abilities and imagination. After a change in the technique of drawing, we observed the consecutive three stages of motor pattern development. We noted an effect of motor pattern changing on fine art creation, which can be useful for practicing art (especially by handicapped artists) or for art teachers. By an analogy between tool changing and the appearance of disability, our findings could be also useful in rehabilitation.

Carotid artery dissection and delayed onset stroke caused by a minor blunt trauma in daily life

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Objective: We present a case of traumatic CCA dissection and delayed onset stroke caused by a minor blunt trauma in a young office worker. **Case Description:** A 29-year-old woman slipped down and bumped against the corner of a table in her workplace. After the trauma, she felt dull pain in the neck without a bruise. Next day, she had mild headache and saw a black spot in front of her eye fields intermittently. However, symptoms got improved immediately. On the third day, dysarthria and left hemiplegia were developed suddenly. Neck CTA showed nearly total long segmental occlusion of right mid to distal CCA. Brain MRI and MRA displayed acute cerebral infarction on right basal ganglia, partial embolic occlusion at distal M1 segment of right MCA, decreased flow related enhancement in right ICA and no visualization of flow related enhancement in right CCA. TFCA revealed thrombotic occlusion of right proximal CCA. There were no abnormal laboratory findings but slightly increased LDL cholesterol and triglyceride. She was diagnosed as CCA dissection and delayed-onset cerebral infarction caused by blunt trauma. She took medication and received occupational therapy for 2 months and showed significant functional improvement except slightly decreased fine motor control of left hand. **Conclusion:** Even a minor blunt trauma that can be accidentally occurred in daily life may cause serious vascular events or stroke. In this case, the probable injury mechanism to the carotid artery might be direct blow and the stretch of carotid artery by neck hyperextension posture.

Quadripareisis and severe cognitive deficits after acute carbon monoxide (co) poisoning - rehabilitation outcomes

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Introduction: Acute carbon monoxide (CO) poisoning occurs after breathing in too much CO and may result in serious neurological manifestations, such as cognitive defects, especially affecting memory and learning, and movement disorders. These disorders are typically related to damage to the cerebral white matter and basal ganglia. Case Report: A young 23-year-old man was admitted to emergency department on 28/02/2013 after poisoning with CO, being comatose [GCS: 5/15 (1-1-3)]. He was intubated and admitted to the ICU, on mechanical breathing support. Initial investigations revealed: metabolic acidosis (pH 7.32), CPK: 21000, rhabdomyolysis and acute renal failure. Tracheostomy was performed on 06/03/2013 and removed on 31/03/2013. Brain MRI showed findings consistent with diffuse ischemic leukoencephalopathy and demyelination foci in the corpus callosum. On admission to our Center (01/04/2013), he presented with GCS: 10/15, quadripareisis and left peroneal neuropathy. He had a nasogastric feeding tube and urinary catheter. His initial FIM+FAM score: 58/210. He followed an intensive rehabilitation program including physical therapy, speech therapy, occupational therapy, hydrotherapy, robotic gait training and psychological support. Results: During his stay, he remained hemodynamically stable and afebrile. He showed significant improvement of neurological status, swallowing disorders and cognitive deficits (MMSE score: 30/30). On discharge (06/08/2013), he was walking without aids, was independent in all ADLs (FIM+FAM score: 200/210). Conclusion: Timely diagnosis, effective treatment and early rehabilitation can improve outcomes for patients with CO poisoning and prevent its complications.

Botulinum toxin injection into salivary glands for promoting swallowing rehabilitation, communication and quality of life in a patient with tracheostomy and severe swallowing disorders post stroke

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Introduction: Swallowing disorders (SD) post stroke may lead to serious respiratory complications and tracheostomy. Botulinum toxin type A injection in salivary glands (BTISG) is a treatment option for sialorrhea, a sign of SD. Purpose: To present a case of a stroke patient with tracheostomy, severe SD and sialorrhea, treated with BTISG. Case report: A 73-year-old man with stroke, admitted to our Center on 25/06/2015, presented with tetraparesis, a tracheostomy tube (TT) and PEG tube due to severe SD. GCS score: 11/15. He followed intensive rehabilitation program, but had several episodes of serious respiratory infections, treated in ICU. Fiberoptic Endoscopic Evaluation of Swallowing (FEES) showed absent gag reflex and aspiration. Chest CT scans revealed trachea dilatation, endoscopically confirmed. A TT of adjustable length with cuff was placed (January 2016). No respiratory infection occurred after March 2016. Mental, physical and mobility status improved significantly. His main complaint was the inability to speak and communicate. Following intensive speech therapy and FEES, a speaking TT was placed (July 2016). Saliva and bronchial secretions remained excessive, but were managed effectively by coughing. Anticholinergics initially used had no results. After BTISG (August 2016), saliva and bronchial secretions reduced significantly, allowing deflating the cuff initially and, finally, capping the tracheostomy for almost 10 hours daily, with no complications, enabling speaking, communicating, participating; improving his mood and quality of life (QoL). Conclusions: BTISG combined with an intensive rehabilitation program resulted in significant improvement of SD, enabling the patient to communicate and participate, thus improving QoL.

Can patients who underwent neurosurgery for gliomas get a significant improvement from rehabilitation?

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Introduction: Patients who underwent neurosurgery are a strong test for rehabilitation units (high length of stay, high resource consuming, poor prognosis). It is still controversial if such patients (most patients with neoplastic disease) can get a significant improvement from rehabilitation. The aim of the study was to evaluate outcome comparing malignant and non malignant patients hospitalized in our rehabilitation unit. **Material and Methods:** We considered 55 patients hospitalized in our rehabilitation unit between March 2011 and July 2016 with who underwent intracranial surgery. Their age was between 20 and 84, with an average of 55.1, SD 14.4. In 34 patients out of 55 (61%) there was no malignancy. 11 (20%) were affected with neoplastic disease with poor prognosis, the remaining with low malignancies. **Results:** The mean length of stay was 60 days \pm 61. The mean delay between surgery and admission was 32 days. Mean modified Rankin Scale ad admission was 4.3 \pm 0.7. At discharge 3.3 \pm 1.3. 32 patients (58.1%) were discharged at home, 2 deceased, 7 were sent to other rehabilitation facilities, the others went back to neurosurgery, neurology or intensive settings. People who went back home had a higher mean GOS: 4 \pm 0.9 (in the others 3 \pm 0.7). Po.001, two tails t test. Modified Rankin Scale at discharge was lower in patients who were discharged home. There was no significant relation between discharge at home and malignancy (chi square test). **Discussions and conclusions:** Our patients can get a significant improvement from rehabilitation, no matter if affected with malignancies or other intracranial pathology.

Cavum septum pelucidum in neurologic patients

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Cavum septum pellucidum (CSP) is a normal variant CSF space between the leaflets of the septum pellucidum. The aim was to evaluate its occurrence with neurologic nosologies. Methods Intrigued by this casually radiological finding we retrospectively analyzed fourteen patients with cavum septum pellucidum among patients admitted with neurological emergencies. Among them 64% were male while 36% female aged from eighteen to eighty years old with mean age of 56. Results Neurologic diagnosis raised commonly were stroke in 42% (recurrent ischemic, lacunars 17% similarly ; 8% pontine lacuna in vasculitis from Bexhet disease), epilepsy in 24% (TLE , epilepsy -dementia, new onset SE Status Epileptic in herpetic temporal encephalitis with 8% respectively), 16% CDH chronic daily headache ; migraine with visual aura or chronic psychosis identically) PD Parkinson Disease 8% , MS (Multiple Sclerosis) 8%. Neurologic objective examination was normal 13%, frontal syndrome 13%, motor impairment 50%, Parkinsonism, psychomotor agitation equally with 8%. (CSP) in imaging resulted associated with 24%, thalamic, basal ganglia and pontin lacuna 24%, cortical atrophy 14%, CSP only 14%, frontal agenesis, left frontal hygroma, white matter demielinissant plaques, temporal posterior brain edema in encephalitis 6% simultaneously. EEG performed in 24% of patients revealed; normal generalized alfa in CDH case, FIRDA in TLE and diffuse intermittent delta in SE case with identical prevalence. Conclusions; CSP resulted coincidentally associated with diverse neurological diseases imaging's frequently observed with in stroke 42%, less subsequently with epilepsy 24% , followed by CDH 16% and lastly concurrently occurred with post-trauma , MS, PD, or vasculitis.

Falls affecting quality of life

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Objectives: Falls are important causes of hospital admissions, injury and even death among the elderly population; people don't fall because they get older. There is more than one underlying cause involved in a fall and often incompletely investigated and treated, affecting the quality of life (QoL) of patients and caregivers. **Methods:** We conducted a prospective study on 71 consecutive patients which were admitted in our clinic as a result of a fall. The mean age was 77 years (61-93). We tried to identify the leading cause for falling and the consequence on QoL. **Results:** The causes for our patients' falls were: stroke, vertigo and balance difficulties, Parkinson's disease, polyneuropathy, vision problems, arthritis and other orthopaedic problems, seizures, postural hypotension, environmental factors. Only 34 patients had a single cause for falls, 37 of them had 2 or more factors that caused falls. Almost all the patients needed a multidisciplinary medical team to pass the consequences of their fall. **Conclusion:** Most falls are caused by a combination of risk factors. Falls, even without any injury, have a psychological impact on patients. They become afraid of falling again. The fear was increased by the number of falls. QoL is affected in the same proportion by the physical consequence of falls (trauma, fractures, haematomas, pain) as well as by anxiety, reducing the motility and activity of the patients and increasing their dependence on caregivers. A multidisciplinary team is necessary to prevent and treat consequences of falls in elderly.

The exoskeleton experience in gait training of neurological patients

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The evolution of technology and its use in the rehabilitation field provide us with new sophisticated tools to achieve the rehabilitation goals. Some of the most innovative systems are the robotic technology systems which help us to use in the best way the patients' abilities. They are usually specialized for gait training. One of the most innovating system for robotic gait training is EXOSKELETON. This system has been used in the facilities of <> Rehabilitation Center for promoting walk abilities of neurological patients. The patients are following a multidisciplinary rehabilitation approach and use of EXOSKELETON is combined with the rest of the program. We have the experience of 4 patients following this combined program (3 stroke and 1 MS patient). They used EXOSKELETON for gait exercise twice a week for 6 weeks. In the advantages are the correct step pattern learned, the faster speed achieved than the conventional therapy, the natural fully weight bearing gait, the task specific gait training and the more customized and intensive (high-dosage and high intensity) gait training. In the disadvantages are the time consuming fit and adjustment of the robotic system, the need for good patient's cooperation and perception, the high cost of the system and the restrictions (spasticity, floor specifications, length limb discrepancy >4 cm, body weight >100 kgr).

Quality of communication in the rehabilitation of persons with aphasia and/or dementia: the caregivers perspective

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We propose that performance on a quality of communication scale for caregivers primarily reflects the communication underpinnings that tap the communication effectiveness of persons in rehabilitation with stroke and/or dementia. Demographic differences as related to illness, sex, age, time of disease and communication disorder were studied. These results support the hypothesized associations between caregivers' perspectives for: 1. daily routines & autonomy, 2. self-perception & personality, 3. social life & and interaction and 4. Cognitive and communication skills and 5. other general questions. Individuals for stroke (Mean=2.94, $p=0.009$ 0.05) as compared to individuals with dementia (Mean=3.37) showed statistically significant differences with regard to self-perception and personality. Moreover, for both groups social life and interaction (3.) was found to be significantly worse, especially for females (Mean=3.96, $p=0.015$ 0.05) as compared to males (Mean=3.44). Both groups with more than 11 years of having either stroke or dementia showed statistically significant differences mean=3.43 ($p=0.028$ 0.05) in the area of cognitive and communication skills however if the speech and language is not effected this result is also significant (Mean=3.27, $p=0.022$ 0.05). Moreover, an analysis of the statistically significant differences between the two groups revealed an intriguing association for two groups of caregivers. Results of this demographic analysis suggest that examining quality of communication from the caregivers' perspective can provide a useful way to bring undefined views of caregivers into closer alignment with the rehabilitation outcomes of communication quality.

The influence of ion-reflex impulsive magnetic electrophoresis on bioelectric activity of the brain

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In recent years, more and more attention of researchers attracted neurostimulatory effect of pulsed magnetic fields, such as transcranial magnetic stimulation. There is information about the increase of the functional activity of clock mechanisms of the brain under the influence of short-term local alternating magnetic field. The aim: To study the effect of ion-reflex impulsive magnetic electrophoresis on bioelectric activity of the brain. Materials and Methods: There was study of bioelectrical activity of the cerebral cortex of 30 relatively healthy volunteers aged 21 to 61 years with the help of electroencephalography recording. The study was carried out three times: before the experiment, after the first magnetic electrophoresis session, third record - at the end of 5 sessions. Results and Discussion: The decrease in the asymmetry of alpha rhythm in the dynamics on the background of magnetic therapy sessions with magnetic electrophoresis. Also an improvement in the frequency parameters of the alpha rhythm from 7.0 to 11.6 Hz is observed in the dynamics. Over both hemispheres, mainly in the fronto-temporal leads registered low- and high-frequency beta rhythm. The activity of beta rhythm by frequency remained 14-35 Hz (prior to treatment 12 to 35 Hz), by amplitude was modulated over 8-35 μ V. Volunteers noted improvement in general well-being, increase in efficiency, improvement of memory, attention, synchronization of circadian rhythms of sleep. Conclusions: The study showed a positive effect of ion-reflex impulse magnetic electrophoresis on the functional state of the brain, as evidenced by the the results of our study that can be used in neurorehabilitation and requires further study.

Age and gender characteristics of the cerebrovascular diseases among patients with type 2 diabetes mellitus**R. Aliyev², S. Mehdiyev¹, I. Mustafayev¹, M. Mammadov³**¹*Department of Therapy, Azerbaijan State Advanced Training Institute for Doctors named after A.Aliyev, Azerbaijan*²*Department of Neurology, Azerbaijan State Advanced Training Institute for Doctors named after A.Aliyev, Azerbaijan*³*Laboratory for Interdisciplinary Approaches on the Prevention of Chronic Non-communicable Diseases, Federal State Institution National Research Center for Preventive Medicine, Russia*

Background. Type 2 diabetes mellitus (2DM) is a major risk factor for cerebrovascular diseases (CVD). Aim. To study clinical and epidemiological features of CVD prevalence in patients with 2DM. Material and methods. 810 patients (31.2% men, 68.8% women) aged 30 to 69 (with the mean age 53.9 ± 0.4 year) were involved to the research. They answered the questions in the "ARIC" international questionnaire, which was prepared by experts of World Health Organization for using in clinical and epidemiological studies. All patients were examined by a neurologist. A carotid dopplerography was implemented and the level of glucated haemoglobin (HbA1c) was identified by express method for all the patients. Results. The questionnaires analysis showed that 12.8% parents of the patients with type 2DM had cerebral stroke under the age of 55 (females – 7.3%, males – 5.5%, $p < 0.05$). Carotid artery stenosis degree was about 40% in 30.1% of patients (males – 2.7%, females – 27.4%, $p < 0.01$), about 50-59% in 57.5% of patients (males – 16.4%, females – 41.1%, $p < 0.05$) and more than 60% in 12.3% of patients (males – 2.7%, females – 9.6%, $p < 0.05$). Carotid intima-media coefficient (IMC) was 1.2 ± 0.5 mm (95% CI 0.4-3.2) on the right side and 1.4 ± 0.6 mm (95% CI 0.6-3.5) ($p < 0.05$) on the left side. The average level of HbA1c was $8.5 \pm 0.3\%$ (men $8.2 \pm 0.3\%$, women $8.8 \pm 0.4\%$) ($p < 0.05$). Inadequate glycemic control was considered as the reason of IMC increase ($p < 0.05$). Conclusion: Frequency of CVD prevalence in 2DM was significantly higher among women than men and it can be explained with non adequate glycemic control.

How many controversies fit in a stroke case?

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Introduction: Stroke is a major cause of death and prolonged disability. Common causes of an ischemic stroke are thrombosis from stenosis or occlusion of large arteries or embolism mainly from cardiogenic sources. Identification of etiology is fundamental in planning treatment strategy and secondary prevention. Case report: A 61 -year-old right handed man was admitted eight hours after the onset of right side hemiparesis ,right hemianopsia and also expressive aphasia. He was getting dabigatran 110mg twice per day for atrial fibrillation. Computer tomography (CT) showed large infraction as a low density lesion in the territory of anterior, middle and at a less degree of posterior cerebral artery with surrounding edema and mass effect. CT angiography revealed an anatomic variant with the left anterior artery to be branch of middle artery and the left posterior to be hypo plastic. Furthermore a severe stenosis, almost 80% of the left internal artery in the neck was detected. He decided to continue his anticoagulation therapy with rivaroxaban 20mg once daily and to perform interventional treatment for the internal carotid stenosis three months later. Discussion: This case includes many dilemmas .Firstly should be expanded the laboratory and imaging work up despite the obvious cause of ischemic stroke? In which cases they should decide so? Moreover a patient under Noacs for atrial fibrillation and a new severe ischemic stroke should continue the same therapy or change with warfarin? Finally what is the best timing and also the best procedure for a severe carotid stenosis in the neck after a major stroke?

A case of widespread cavernous angiomas of the central nervous system associated with acute neurologic deficit

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Background: Multiple cavernous angiomas(CA) in the central nervous system (CNS) are commonly associated with family history of CAs or previous radiation therapy on the CNS. In addition, neurologic deficit by spinal cavernous angioma more chronically appears in the adults compared than the children in which a rapid progression of the neurologic deficit associated with bleeding of CAs. Here in, we introduce a rare case in which a woman without familial or radiation history appeared with acute neurologic symptoms resulted from multiple CAs. Case Report: A 45-year-old female visited our clinic due to sudden right leg weakness and sensory loss. Brain and spinal cord magnetic resonance imaging showed widespread CA. CA in L1 spine level was accompanied by a hematoma of subacute stage with perilesional edema. Sensory loss was subsided after corticosteroid therapy. Conclusion: Diffuse involvement of CNS of CAs is rare condition without family history of CA and previous radiation therapy on the CNS. In conclusion, as in the present case, acute neurologic deficit can be associated with diffuse CAs in the CNS and extensive neuroimaging evaluation is needed to identify symptomatic CAs.

Cerebral hyperperfusion syndrome: a preventable and treatable cause of seizures

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Introduction: Cerebral hyperperfusion syndrome (triad of headache, seizures and focal neurological deficits), which occurs in 0.2 to 18% post-carotid endarterectomy, is a preventable complication. Case report: A 63 yr old female with hypertension, hyperlipidemia and diabetes mellitus presented with acute left lower limb weakness. Home BP ranged from 104-146/43-94 mm Hg. Neurological examination revealed left lower limb monoparesis. MRI Brain showed acute right parasagittal frontoparietal infarcts. CTA neck showed severe stenosis at the proximal right ICA with tiny right ACA / PCA and watershed infarcts. She underwent successful carotid endarterectomy ten days later. Postop BP ranged from 114-154/65-102 mm Hg. A week later during rehabilitation, she developed recurrent left focal seizures. This was preceded by severe headaches the night before. CTA / CT perfusion revealed increase in perfusion in the right MCA territory secondary to postop hyperperfusion. The operated ICA site was patent and there were no new infarcts. EEG revealed right PLEDS. She was treated with anticonvulsants and BP control was achieved with IV labetalol, captopril and atenolol (kept less than preop BP). To-date she remained well with no complications. Discussion: Cerebral hyperperfusion syndrome can occur immediately postop to one month later. Pathophysiology involves impaired cerebral blood flow autoregulation with elevated systemic hypertension and vasogenic white matter edema. Prevention is key and numerous risk factors (preop, perioperative and postop) for development of this syndrome have been identified. Close hemodynamic monitoring is needed in patients with risk factors. TCD may be used for monitoring. Conclusion: Clinicians should be aware of this potentially preventable post carotid endarterectomy complication

Driving risk after stroke

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Abstract: [Purpose] The aim of this study is to evaluate patients with confirmed stroke, using the DriveABLE Cognitive Assessment Tool (DCAT) to predict their driving risk. [Subjects and Methods] A total of five hundred and fifteen patients were tested from July 1st, 2015- June 30th, 2016, out of five hundred and fifteen patients, one hundred and eight confirmed stroke patients participated in this study. A 1-year retrospective study was conducted in a Neurology clinic. A medical student, attending physician and staff, conducted DCAT evaluations, data gathering and statistical analysis. All participants were classified into the safety or risk groups based on the DCAT results. [Results] Seven patients (6.48%) were within range of normal, 17 (15.74%) patients' cognitive abilities maybe affected, 22 (20.37%) cognitive abilities of driving are affected and 62 (57.4%) were outside the normal range and are not suitable to drive. [Conclusion] The DCAT is a helpful tool in assessing the driving risk of stroke patients. Key words: Driving, Stroke, DriveAble Cognitive Assessment Tool.

Controversies of thyroid dysfunction effects in patients with acute ischemic stroke

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Background: Previous studies showed that thyroid dysfunction is associated with more stroke severity and poorer functional outcome. However, there are controversies about the effects of particular thyroid hormones. Methods. 124 adult patients with acute ischemic stroke were included in this study. Exclusion criteria were autoimmune thyroiditis or thyroid carcinoma. Concentrations of free T3 (fT3), free T4 (fT4), TSH, as well as stroke risk factors were assessed during 24h from symptoms onset. Levels of thyroid hormones below 25 and above 75 percentiles were accepted as low and high respectively. Neurological deficit was assessed by Scandinavian Stroke Scale (SSS). Results. Analysis showed that patients with high fT3 levels (≥ 5.35 pmol/l, 95% CI 5,01-5,61) had less severe stroke compared to other patients (SSS median 44.5 vs. 36, $p = 0,0418$). This effect was stronger in the subgroup of patients without prior stroke or TIA (SSS median 48 vs. 37, $p = 0,0148$). Multiple regression showed that fT3 level had influence on the risk of disabling deficit (mRs score ≥ 3 at 6 month after stroke) independently of gender, age, stroke risk factors and etiology (OR=0.6389, 95% CI 0,4173 to 0,9782). There was no connection between fT4 and TSH concentrations and stroke severity or functional outcome. Conclusion. This study confirmed that low fT3 levels are associated with greater neurological deficit and poorer outcome in stroke patients. Higher levels of fT3 seemed to play a protective role. Future studies should be aimed at assessing the possible positive effects of additional fT3 supplement during stroke.

Anticoagulant therapy and unruptured intracranial aneurysm

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Introduction: Data on anticoagulant therapy (AT) in patients with cardioembolic stroke and unruptured intracranial aneurysm are scarce. Decision is predominantly made by calculation of spontaneous aneurysm rupture and risk of recurrent stroke. Case report: 69-years old female with a paroxysmal atrial fibrillation was admitted to our hospital due to acute left-sided hemiparesis. Head computed tomography (CT) showed two hyperdense lesions in right thalamus. CT angiography showed no neck vessels stenosis and a 4 mm unruptured aneurysm on a.communicans anterior. Preventive LMWH and Aspirin were initiated. Control CT scan 5 days latter showed haemorrhagic transformation (HT) of ischemic stroke in right parietotemporal lobe, which was confirmed also by MRI scan. Due to haemorrhagic transformation AT was postponed. CT scan 6 days latter showed progression of haemorrhagic transformation. Aspirin was ceased. She completely neurologically recovered during hospitalisation (NIHSS 0). CT scan 3 weeks latter showed complete resorption of HT. AT with dabigatran in a lower dosage was initiated. She was latter on admitted to a cardiologist for an opinion of left atrial appendage occlusion (LAA) implacement. Conclusions: There are no guidelines on AT in patients with cardioembolic stroke and unruptured intracranial aneurysm. Data on higher probability of aneurysm rupture due to AT is unknown. Decision on AT initiation is made on calculation of probability of spontaneous aneurysm rupture and risk of recurrent stroke. Initiation of lower dosage AT or LAA implacement could be treatment options in our patient.

Can ischemic preconditioning make spinal cord resistant to infarction?

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We present the longitudinal clinical and electrophysiological study of 41 patients with spinal stroke and 25 patients with vascular chronic myelopathy. Thirty healthy subjects were considered as a group of references. All cases were confirmed by MRI examinations. Electrophysiological examination included needle electromyography, sensitive and motor electroneurography, F-wave study, Hoffmann reflex and motor-evoked potentials. In spinal stroke patients three vascular syndromes were considered: anterior spinal artery syndrome, syndrome of complete transversal lesion and posterior spinal arteries (artery) syndrome. The patients with chronic ischemic myelopathy were divided in several groups according to dominant clinical syndrome: spastic, spastic-atrophic and atrophic. Clinical and electrophysiological findings were assessed in each case together with etiological factors and the level of ischemic spinal lesion. Electrophysiological abnormalities were founded in 100% of cases. Based on statistical analysis of the results, electrodiagnostic criteria were elaborated for the discrimination of each syndrome of spinal stroke and chronic ischemic myelopathy. In addition to this data were founded that chronic ischemic damage of spinal cord tissue causes functional reorganization of motor units. Moreover, as a result of ischemic preconditioning and neuronal plasticity at the level of spinal cord new program of motor function was established. The general conclusion of this work is that multimodal electrophysiological investigation as a consciously extension of clinical examination can give important arguments that ischemic preconditioning protect spinal cord to infarction.

Left ventricular outflow tract endocarditis: an unusual cause of multiple brain embolisms

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OBJECTIVES: Neurological complications arise among 15 and 30% of patients with infective endocarditis. We aim to describe an unusual cause of septic embolisms. **METHODS:** We present a 50-year-old woman with previous arterial hypertension. She was admitted due to abrupt onset of fever, confusional state, and papular-erythematous spots located on the trunk, face and extremities. Cerebrospinal fluid analysis revealed 142 white blood cells per mm³ (96% neutrophils) with a negative Gram stain, 58.2 mg per dl of protein, and a normal glucose level. Empirical antimicrobial therapy was initiated. Brain magnetic resonance imaging showed multiple cortico-subcortical embolic lesions, located in both cerebral and cerebellar hemispheres and basal ganglia, as well as a mild leptomeningeal enhancement. In a transthoracic echocardiography, neither vegetations nor valve dysfunction were observed. **RESULTS:** Two days after admission our patient presented an acute coronary syndrome with ST elevation. A transesophageal echocardiography identified a rounded 1 cm² echogenic mass anchored into left ventricular outflow tract (LVOT) endocardium, contacting with anterior mitral leaflet during diastole. Blood cultures were positive for Methicillin Sensitive Staphylococcus Aureus (MSSA). Due to clinical evolution and the inability to control septic emboli, the patient underwent emergency surgical removal of the intracardiac mass. The postoperative course was uneventful with no neurological deficits at discharge. **CONCLUSION:** LVOT is an infrequent location of abscesses and vegetations and their embolisms are commonly difficult to control. In case of brain embolisms without severe clinical impairment, surgery should not be delayed. Early surgical treatment significantly reduces mortality, without increased risk of new neurological events.

The comparison of procedural characters and clinical outcome between Solitaire stent and Trevo stent in Endovascular treatment for acute ischemic stroke

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Background: To compare the safety and effectiveness of two retrievable stent systems in EVT for AIS using Solitaire and Trevo. Methods: Patients were treated either with Trevo stent or Solitaire Stent according to the neurointerventionist preference. Recanalization was classified by TICI grade. Efficacy and safety during EVT were analyzed the rate of good recanalization after the first pass, clot retrieve rate, final recanalization grade, and use of rescue method, recanalization time, hemorrhagic complication and thromboembolic complication. Results: Seventy-nine patients were treated with Solitaire stent and 51 with the Trevo stent. Overall good recanalization (TICI 2b and 3) was achieved in 57 patients (72.2%) in the solitaire group and 46 (90.2%) of the Trevo group ($P = 0.01$). The rate of good recanalization after the first pass, clot retrieve rate were not significant between two groups. However, use of rescue method was more frequent in Solitaire group. Good clinical outcome was higher in Trevo group, but not significant. The rate of symptomatic ICH and thromboembolism were not significantly different. Conclusions: Our study showed several superiorities of Trevo stent compared with the Solitaire stent in EVT. Trevo stent showed superiority to achieve more successful recanalization, less use of rescue method, less take a time for recanalization. Even though the clinical outcome was not different between two stentriever, we think that Trevo stent would be better stentriever in EVT

The effect of Induced hypertensive therapy in acute ischemic stroke patients with steno-occlusive disease and hemodynamic instability

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Objectives: Induced hypertensive therapy (IHT) has used to enhance cerebral perfusion pressure in subarachnoid hemorrhage and stroke, but there is no established indication for IHT in ischemic stroke. We report the usage of IHT in acute ischemic patients with hemodynamic instability caused by steno-occlusive disease of a main cerebral artery. **Method:** We reviewed acute ischemic stroke patients with cerebral perfusion deficit due to intracranial and extracranial steno-occlusive disease. IHT was applied for early neurological deterioration and maintained until hemodynamic instability was stabilized over 24 hours or neurointervention including angioplasty and extracranial intracranial arterial bypass surgery were performed. **Result.** 52 patients were analyzed. Territories of stroke were 31 of anterior circulation of intracranial vessels, 11 of posterior vessels, and 10 of extracranial vessels. Mean duration of IH therapy was 4176.04 minutes. Pre and post NIHSS score of IH therapy was 8.19 and 7.35, respectively. 30 patients (57.7%) were showed improvement and 13 patients (25%) were stabilized without further aggravation. 16 patients revealed bradycardia. There was no fatal complication of therapy. 15 patients were performed further treatment include bypass surgery, angioplasty, and stenting after IH therapy. At 3 months follow up, 34 patients showed good outcomes (modified Rankin scale 0, 1, and 2). **Conclusion:** IHT may be safe and effective for the neurologic deterioration or progression of acute ischemic stroke with hemodynamic instability due to severe steno-occlusive disease of major cerebral artery. Large randomized trials are needed to confirm this result.

Do geographical considerations and patient volume argue to convert a primary into a comprehensive stroke center

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Background: No comprehensive study exists about Mechanical Thrombectomy (MT) accessibility for patients admitted to a primary stroke center (PSC) without on-site interventional neuroradiology service. **Aims:** To evaluate MT accessibility within 6 hours after transfer from a PSC to a distant (1.5 hour by car) comprehensive stroke center (CSC). **Methods:** 3-year prospective registry of patients admitted to a PSC within 4.5 hours after symptom onset selected for transfer to a CSC for MT. Eligible patients had confirmed proximal arterial occlusion and no large cerebral infarction on MRI (DWI-ASPECTS ≥ 5). The rate of transfer, transfer without MT, MT, reperfusion (TICI score $\geq 2b-3$) and main relevant time measures were determined. **Results:** Among the 385 patients selected for intravenous thrombolysis (IVT) and/or potential MT, 211 were considered as transferrable for MT. The rate of transfer was 56.4% (n=119/211), transfer without MT 56.3% (n=67/119), MT 24.6% (n=52/211) and overall reperfusion 18% (n=38/211). The relevant median times (interquartile range) were: 130 minutes (62) for IVT start to CSC door, 95 minutes (39) for PSC door-out to CSC door-in, 191 minutes (44) for IVT start to MT puncture, 354 minutes (107) for symptom onset to MT puncture and 417 minutes (124) for symptom onset to recanalization. **Conclusions:** Our study suggests that transfer to a distant CSC is associated with reduced access to early MT in patients with acute ischemic stroke and large artery occlusion. These results could be translated to other high volume distant PSC.

Acute ischemic stroke in moyamoya disease caused by thyrotoxicosis: A case report

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Background & Significance: Moyamoya disease is a progressive cerebrovascular disorder of unknown cause, characterized by bilateral stenosis or occlusion of the arteries around the circle of Willis with prominent arterial collateral circulation. Moyamoya syndrome has rarely been reported in association with Graves` disease. Several studies suggest that an ischemic stroke might have occurred in patients with thyrotoxicosis. **Case:** A 41-year-old woman presented with dysarthria and aphagia. She also had episodic transient right arm weakness. Brain magnetic resonance(MR) imaging revealed an acute infarction in the territories of left anterior cerebral artery and middle cerebral artery. MR angiography showed total occlusion of both internal carotid arteries, anterior cerebral arteries and middle cerebral arteries. Thyroid function tests revealed thyrotoxicosis, with a TSH level of 0.01 uIU/mL, a T3 level of 523 ng/dL and a free T4 level of 9.08 ng/dL. After antithyroid medication, the patient`s symptoms improved. **Conclusion:** Thyrotoxicosis due to Graves` disease is harmful to arterial walls because it may alter vascular reactivity and frequently provoked cerebral vasospasm. Therefore, thyrotoxicosis can be a cause of ischemic stroke and aggravate neurologic symptoms in the patient with Moyamoya disease.

Association between malignant middle cerebral artery infarction and brain natriuretic peptide levels in stroke patients with atrial fibrillation

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Background and objective: Ischemic stroke with atrial fibrillation (AF) leads to large infarction and severe neurological deficits. However, clinical characteristics associated with malignant middle cerebral artery infarction (MMI) in acute stroke patients with AF have not been previously reported. This study was aimed to elucidate the factors correlated with MMI in stroke with AF. **Methods:** Consecutive patients with acute ischemic stroke and AF who underwent magnetic resonance image within 24 hour from onset were retrospectively enrolled. Patients with posterior circulation stroke were excluded. All patients were divided into MMI and non-MMI groups using MMI definition of a National Institutes of Health Stroke Scale score 15 and infarct volume 82 cm³ on initial diffusion-weighted imaging or ischemic signs 50% of the MCA territory on follow-up brain computed tomography. Multivariate regression analysis was used to identify factors associated with MMI. **Results:** A total of 142 patients were included and MMI was found in 31% of the patients. In univariate analysis, patients with MMI were older and had higher D-dimer and brain natriuretic peptide level. On multiple logistic regression analysis, earlier onset-to-image time (OR 0.85, 95% confidence interval [CI] 0.73-0.98, P=0.025 for 1 hour) and higher brain natriuretic peptide level (OR 1.22, 95% CI 1.07-1.39, P=0.003 for every 100 pg/mL) were independently associated with MMI after adjustment for potential confounders or mediators. **Conclusions:** Plasma brain natriuretic peptide level and onset-to-image time are independently associated with MMI among patients with stroke and AF.

Novel locus-specific genetic characteristics in cadasil

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Objective: We evaluated whether specific gene locus are related to clinical phenotypes. **Methods:** We screened patients with a suspected diagnosis of Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) between 2005 and 2015. Mutational hotspots of the Notch3 gene in exons 2-23 were screened by using Sanger sequencing. We analyzed magnetic resonance imaging (MRI) in those patients. **Results:** A total of thirty four patients (women, n=21 and mean age, 52±10 years) were included in our study. The majority of the mutations were in exon 3 and exon 11. The most prevalent mutations were R75P mutations (n=5), followed by Y465C (n=4) and R544C (n=4). Patients with those mutations exhibited less frequent anterior temporal (AT) or external capsular (EC) hyperintensities compared to patients with other locus mutations. Hemorrhagic stroke was found to be associated with mutations in exon 3 (R75P), exon 9 (Y465C), exon 11 (R587C) and exon 22 (R1175W variants). **Conclusions:** In contrast to westernized countries, CADASIL patients in our study frequently had mutations in exon 3 (R75P) and exon 11, and they did not have typical AT or EC hyperintensities. Although the underlying genetic mechanisms remain unclear, we suggest that some CADASIL mutations appear to have locus-specific characteristics.

Diabetes decreases hippocalcin expression in focal cerebral ischemia

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Stroke is a major cause of disability and death in adults. Hyperglycemia causes intracellular calcium imbalance after ischemic insult, aggravates cytochrome c release into cytosol and activates caspase-3, and ultimately triggers apoptosis. Hippocalcin is a neuronal calcium-sensor protein that acts as a calcium buffer to regulate the intracellular concentration of Ca^{2+} . This study was investigated to elucidate hippocalcin protein expression of the cerebral cortex during ischemic brain injury between non-diabetic and diabetic animals. Adult male rats were injected with streptozotocin (40 mg/kg) via the intraperitoneal route to induce diabetes and underwent surgical middle cerebral artery occlusion (MCAO) 4 weeks after streptozotocin treatment. Cerebral cortex tissues were collected 24 h after MCAO. A proteomic approach and Western blot analysis revealed that hippocalcin protein was significantly decreased in diabetic animals with MCAO injury compared to diabetic-only and MCAO-only animals. The decrease of hippocalcin in hyperglycemic condition suggest that hyperglycemia leads to intracellular calcium imbalance by regulating hippocalcin expression levels in ischemic brain injury.

“Inflammatory parameters and their association with stroke volume and localization in acute ischemic stroke patients: a three month pilot study.”

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Background: The important pathophysiological role of inflammation in acute ischemic stroke (AIS) is indisputable, although the results of recent studies concerning the relation between several inflammatory markers and stroke volume (SV) as well as localization (SL) are controversial. This pilot study was designed to assess the association of specific inflammatory parameters with SV/SL in AIS patients, based on reliable and easy to perform methods. Methods: Nineteen patients with AIS without signs of active infection or systematic disease were recruited from an inner-city hospital's neurology department in Athens, Greece, during a three-month period. Demographic and clinical data, mainly concerning vascular risk factors and metabolic profile, were collected. SL, supra- or infratentorial respectively, was determined by radiological findings whereas SV was estimated on Diffusion Weighted Imaging (DWI) by ABC/2 technique. Levels of C-reactive protein (CRP), White Blood Cells (WBC), body temperature (BT), ferritin and Erythrocyte Sedimentation Rate (ESR) were collected. Results: According to SL, statistically significant association was observed between infratentorial strokes and higher levels of CRP ($p=0.001$) and ferritin ($p=0.022$), but performing multiple regression revealed only borderline significant association ($p=0.066$) between infra- SL and CRP levels. As SV concerns, statistically significant association was observed between higher SV and elevated levels of BT ($\rho=0.712$, $p=0.001$), ferritin ($\rho=0.450$, $p=0.022$) and ESR ($\rho=0.487$, $p=0.022$), but only the correlation between SV and BT was finally confirmed by multiple regression. Conclusion: Our study supports the assertion that higher SV and infratentorial SL are associated with elevated inflammatory parameters in AIS and are of clinical importance.

Association of red blood cell distribution width with stroke and 5-year cerebrovascular and cardiovascular mortality in young patients with diabetes

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Background: Red blood cell distribution width (RDW) is a measure of erythrocyte anisocytosis that has been recently associated with myocardial infarction, stroke and all-cause mortality. Nevertheless, no study has researched the association of RDW with stroke and cardiovascular mortality in young diabetic patients. Methods: All diabetic patients aged 16-55 years, presenting with an ischemic stroke at the University Hospital Centre "Mother Theresa", Tirana, during 2010-2011 were enrolled. Each patient was matched by age and gender with three stroke-free diabetic controls. Exclusion criteria were hematologic, infectious, inflammatory, autoimmune and malignant diseases. At baseline, the RDW cut-off value of 14% was used to discriminate between the two groups of stroke patients. After a 5-year long follow-up period, cerebrovascular mortality and cardiovascular mortality were assessed either physically or by phone interview in both groups. Results: In the final analysis were included 42 diabetic patients (83.3% males), mean age 47.2 years (SD 6.18) and 126 stroke-free diabetic controls. RDW was significantly higher in stroke patients ($14.27\% \pm 1.1\%$ vs $13.82\% \pm 1.1\%$, $p = 0.023$). During follow-up of stroke patients, higher cardiovascular and cerebrovascular mortality was registered in the higher RDW group ($\geq 14\%$) compared to the lower RDW group (14%), respectively 9 vs. 1 cerebrovascular deaths ($p=0.042$) and 6 vs. 2 cardiovascular deaths ($p=0.029$). Conclusions: RDW is associated with higher risk for ischemic stroke in young patients with diabetes. Moreover, higher RDW at baseline is associated with higher 5-year cerebrovascular and cardiovascular mortality.

Dose serum D-dimer in Non-cardioembolic Ischemic Stroke have clinical prognostic value?

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Background: Although D-dimer levels are significantly associated with cardioembolic infarction, the significance of D-dimer levels in relation to the severity and functional outcomes of other stroke subtypes, such as lacunar and large artery atherosclerosis (LAA) infarction, remains unclear. The purpose of this study was to evaluate whether elevated initial D-dimer levels are significantly and cross-sectionally associated with poor functional outcomes at each time point during a nine-month follow-up period. We also investigated the significance of D-dimer levels in longitudinal temporal changes of functional outcomes in these patients. Methods: We recruited 146 patients with lacunar infarction and 161 patients with LAA infarction who were consecutively admitted to our hospital after acute stroke. Serum D-dimer levels were evaluated initially and the modified Rankin scale (mRS) were measured initially and at 1-month, 3-month, 6-month, and 9-month follow-up visits. Results: Patients with higher D-dimer levels had significantly worse initial functional outcomes, and these worse outcomes were maintained throughout the 9-month follow-up period compared to the low D-dimer group. However, regardless of stroke subtype, D-dimer levels did not influence long-term changes in functional outcomes over the 9-month follow-up period. Conclusion: This study suggests that elevated D-dimer levels can be used as a surrogate marker for poor functional outcomes only during the acute stage. Further evaluation of serum D-dimer levels could provide a helpful predictive marker for stroke prognosis.

Using upper case letters to improve alexia

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Our hypothesis is that individuals with aphasia will be more accurate word readers when the first letter is uppercase rather than letters are all small print. Unlike word reading, non-word reading is phototactically regular and may look like targets in that paraphasic errors or neologisms may be present when reading errors occur. Target items included reading real words and pseudo- words (2,3,4 words stimuli). 2 female and 7male individuals with a medical diagnosis of ischemic left hemisphere stroke and presented with a clinical diagnosis of aphasia of different classifications (2 expressive, 3 mixed type, 2 anomic, 1 global). Eight participants presented with alexia and one with alexia without agraphia and were between the ages of 46 and 80 (Mean=66.2). Participants trained daily and met with the experimenter 2x a week for a supervised 45-minute clinical session. The other homework sessions mirrored these and the experimenter monitored participants progress weekly. A multiple baseline design of 2,3,4 syllable word lists respectively. Pseudo-word reading therapy tasks was also used to prevent carryover effects at the end of each training session daily. Results of a t-test repeated sample showed reading performance were found to be significantly improved in real word reading vs non-word reading with first letter as uppercase across 2,3,4 syllable words ($p=0.044$, $.05$) as compared to all lower-case letters but not for pseudo word reading ($p=.062$ $.05$), respectively. Three of the nine subjects returned to normal levels of reading. Discussion also describes differences between non- word reading and word reading.

Anatomical cause of gerstmann like syndrome identified through mr dti tractography

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Introduction: The symptom complex of finger agnosia, right-left disorientation, dysgraphia, and dyscalculia constitutes Gerstmann's syndrome. Gerstmann syndrome is usually caused by acquired lesions of the dominant parietal lobe including the angular and supramarginal gyri. We describe a patient who exhibited dysgraphia, acalculia, finger agnosia, left-right disorientation as well as anomia and was found to have cortical ischemic lesions in the dominant parietal lobe both through brain MRI and MR Diffusion Tensor Imaging(DTI) Tractography. **Case:** A 56 year old woman, smoker with a history of arterial hypertension and uterine fibroids was brought to the emergency department because of an episode of sudden loss of consciousness. Blood tests revealed low hematocrit and hemoglobin values and the patient was admitted to the Hematology clinic where the diagnosis of acute myelomonocytic leukemia was made. Neurological examination showed an intact level of consciousness, fluent paraphasic speech and the symptom complex of Gerstmann Syndrome. MR angiography identified a 80% stenosis of the left medial cerebral artery and head Diffusion Weighted(DW)-MRI showed multiple acute cortical and subcortical infarcts in the area of distribution of the left medial cerebral artery. The patient's symptoms were weighted with the Boston Diagnostic Aphasia Examination (BDAE) and the anatomic lesion was identified through an MR DTI Tractography. **Discussion:** MR DTI Tractography can visually represent complicated neural networks formed by short connections among different cortical and subcortical regions. In our case, we managed to interpret an unusual complex of symptoms and identify the anatomical cause of a rather rare clinical case.

Endovascular thrombolytic therapy in acute ischemic stroke patients with current malignancy

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Backgrounds & Purposes: Cancer causes a hypercoagulable state, increasing the risk of thromboembolic events including acute ischemic stroke. The safety of reperfusion treatment for acute ischemic stroke in patients with cancer is not well established. Intravenous thrombolysis appears to be safe in patients with cancer. There are no previous detailed reports of endovascular thrombolytic therapy in this population. We investigated the outcomes of endovascular reperfusion treatment for acute ischemic stroke patients with current malignancy. **Methods:** We have recruited acute ischemic stroke patients with active cancer who were treated with endovascular therapy between 2011 to 2014 from stroke registry of Chonnam National University Hospital. Baseline characteristics, radiological findings and clinical outcomes were analyzed. **Results:** Total 10 patients were recruited. Three patients were administered endovascular therapy with intravenous thrombolysis, seven patient underwent only endovascular treatment. Symptomatic intracerebral hemorrhage was observed in 1/10 (10%) and petechial hemorrhage observed in 1/10 (10%). Five patients showed significant improvement in National Institute of Health Stroke Scale score at discharge and modified Rankin scale at 3 months (5/10, 50%). Two patients had no change in National Institute of Health Stroke Scale score and modified Rankin scale at 3 months and 3 patients dead after 3 months. Unfavorable prognosis was observed in patient who received intravenous thrombolysis concomitant with endovascular treatment. **Conclusion:** In carefully selected patients, endovascular treatment may be considered in the management of acute ischemic stroke patients with current malignancy.

Brainstem cavernous malformations: Conservative or surgical approach?

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Cavernous malformations (CMs) are low-flow vascular lesions with an incidence of 0,4-0,8%. 20-35% are infratentorial with a predilection for the pons. Although frequently incidental, they can cause intracranial hemorrhage and focal neurological deficits. No clear consensus exists on whether CMs should be managed conservatively, surgically or with radiosurgery. We present the case of a 66-year old female who was referred for neurological evaluation due to recent onset double vision. She had a history of hypothyroidism and atrial fibrillation. Neurological examination revealed right abducens palsy. Brain MRI and MRA demonstrated a cavernous angioma of the right pons with intralesional bleeding. She received oral dexamethasone with a tapering regimen, showing full remission. There is a long-standing controversy on the optimal approach to brainstem cavernomas. A minimal consensus holds for incidental lesions where surgical-associated morbidity argues for conservative management. Radiosurgery, although presented as a treatment option, is not recommended. Regarding surgical treatment no clear consensus has been reached. Infratentorial CMs seem to have an increased risk of hemorrhage (3.8% per patient-year). This rate is further elevated in patients initially presenting with hemorrhage, those with deep CMs and female sex. Conversely there is a temporal decline in the hemorrhage risk within 2 years (up to 0.8%). This effect is influencing treatment options because the risk of hemorrhage and neurological deficit may decline based on natural history alone. Several studies propose surgical removal in cases of progressive neurological deficit, after the first clinically significant hemorrhage in noneloquent areas or after the second clinically significant hemorrhage in eloquent areas. No level A evidence exists and management still relies on clinical judgment. In our patient we chose a conservative approach under close future surveillance but more studies are warranted to form a reliable treatment algorithm.

VKA: Optimal anticoagulation for secondary stroke prevention of NVAF patients with good (66%) TTR

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Time in therapeutic range (TTR) is the major determinant of adequate anticoagulation for atrial fibrillation (AF) patients on vitamin K antagonists (VKA). Whereas in patients with TTR<66% non-VKA anticoagulants (NOACs) are generally preferred for eligible patients, patients with efficient INR control (TTR≥66%) have a marginal benefit from switching to NOACs. Since there is no randomized controlled trial (RCT) of any NOAC comparing it to patients on VKA with TTR≥66%, we have to rely on pooled data from the existing NOAC RCTs. There seems to be an absolute risk reduction in stroke or systemic embolism with NOACs versus VKA that is inferior to 1%; this benefit is further mitigated in centers with TTR<66%. In these same centers no significant difference in major hemorrhage is noted between NOACs and VKA. Advising in favor of switching of patients already on VKA with an efficient INR control to NOACs is a decision that would have minimal impact on efficacy and no impact on safety according to the limited and indirect, thus moderate-quality, data at our disposal. This choice concerns not only clinicians but also health-care policy makers as the financial burden of such a scenario seems unbearable for most, if not all, health care systems worldwide.

Is there therapeutic effect of Argatroban in Cerebral Territory Infarction?

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Background: Therapeutic efficacy of argatroban is globally not known yet because few clinical studies in acute ischemic stroke are reported and the sample sizes of these studies is small. The aim of this study is to demonstrate an efficacy and safety in patients with cerebral territory infarction who received argatroban within 48 hours from symptom onset. Methods: This study included patients with acute cerebral territory infarction within 48 hours after stroke onset. All subjects were divided into 2 groups: those receiving argatroban on admission (argatroban group), and those receiving aspirin only (control group). We estimated the subjects' neurologic deficits and functional outcomes by using National Institute of Health Stroke Scale (NIHSS) and modified Rankin scale (MRS) prior to argatroban infusion and aspirin administration, on first day and 10th day after initiation of the therapy. Results: In comparison to the aspirin group, the argatroban group showed significant improvement of NIHSS and MRS among before treatment, first day and 10th day after treatment. There was a significant difference of NIHSS and MRS between the argatroban group and the control group at 10th day after initiation of the therapy, which proved superiority of the argatroban group with cerebral territory infarction within 48 hours after stroke onset. Discussion: The present study suggests that argatroban has added benefit in early neurological outcomes after acute cerebral territory infarction and provides safe anticoagulation in acute cerebral territory infarction.

Thrombus in superior vena cava as a cause of venous stroke

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Thrombosis of superior vena cava is a common complication of malignancy, some cardiac and inflammatory diseases, and others. The most common symptoms are swelling of face, arms and chest-wall (87.6%) with associated venous congestion over these areas. We present a case of the patient with thrombosis of superior vena cava resulted in venous stroke. 71 years old man presented in ER with hemianopsia, somatosensory and visual hemineglect right side and confusion. In history the patient had paroxysmal atrial fibrillation, arterial hypertension and upper respiratory tract infection. Brain CT showed cerebral small vessel disease. On ultrasound small atheromatous plaques in both carotid arteries without hemodynamic abnormalities in extra and intracranial arteries were seen. On carotid examination however the abnormally enlarged right jugular vein and thrombosis with total occlusion of left jugular vein were found. Brain MR DWI/ADC showed ischemic focus in left occipital lobe accompanied by incomplete thrombosis of left sigmoid sinus and no flow in left jugular vein. Venous infarct was diagnosed. Hypokinetic right ventricle wall on transthoracic echo and thrombosis of superior vena cava with incomplete obstruction of venous lumen on transoesophageal echocardiography were found. Warfarin was administered. On one month follow-up there was echogenic blood with slow flow in left jugular vein and diameter of right jugular vein has been diminished. No neurological symptoms were present except of somatosensory hemineglect right side. On work-up no predisposing diseases were found. In a patient with common vascular risk factors a less common cause of stroke should be taken into account.

Focal low and global high permeability predict the possibility, risk, and location of hemorrhagic transformation following intra-arterial thrombolysis therapy in acute stroke

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Background and Purpose: K^{trans} , which reflects blood-brain-barrier permeability(BBBP), is influenced by circulation and measurement conditions. We hypothesized that focal low BBBP values can predict the spatial distributions of hemorrhagic transformation(HT), and global high BBBP values can predict the likelihood of HT. **Patients and Methods:** We retrospectively enrolled 106 patients with hemispheric stroke who received intra-arterial thrombolytic treatment. K^{trans} maps were obtained using first-pass perfusion CT data. The K^{trans} values at the region level, obtained using the Alberta Stroke Program Early CT Score (ASPECTS) system, were compared to determine the differences between the HT and non-HT regions. The K^{trans} values of the whole ischemic region based on baseline PCT were obtained as a variable to predict HT possibility at the patient level. **Results:** Of a total of 106 patients, 48 (45.28%) had HT and 21(19.81%) had symptomatic intracranial hemorrhage(sICH). At the region level, there were 72 regions of interest(ROIs) with HT(mean K^{trans} : $0.49\pm 0.53/min$). The mean K^{trans} value of 615 non-HT ROIs was $0.69\pm 0.61/min$, which was significantly lower than that in the non-HT regions ($P=0.0066$). At the patient level, there was significant difference($P=0.0113$) between the K^{trans} values of patients with sICH(1.31 ± 0.88) and without sICH(0.76 ± 0.37). Only a high K^{trans} value at patient level could predict the occurrence of sICH ($P=0.001$; OR:5.040, 95%CI:2.009-12.651). **Conclusion:** Global high K^{trans} values can predict the likelihood of HT or sICH at the patient level, whereas focal low K^{trans} values can predict the spatial distributions of HT at the region level.

The different faces of the p.A53T alpha-synuclein mutation: a screening of Greek patients with Parkinsonism and/or dementia

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Introduction: 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.

Datscan imaging in p.a53t α -synuclein-associated Parkinson's disease: comparison with sporadic Parkinson's disease

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Objective: The objective of this study was to assess striatal dopaminergic denervation in a cohort of symptomatic carriers of the p.A53T α -synuclein (SNCA) mutation as compared to sporadic PD (sPD). **Methods:** DaTSCAN SPECT imaging was acquired at Parkinson's Progression Markers Initiative (PPMI) imaging centers as part of the PPMI imaging protocol and sent to imaging core for processing and calculation of striatal binding ratios. Data from the PPMI database of 10 symptomatic p.A53T SNCA mutation carriers who underwent DaTSCAN at our site, were compared to those of 21 age-, gender- and disease duration- matched sPD patients. **Results:** The striatal dopaminergic denervation was so severe in 3/10 p.A53T mutation carriers, that corresponding binding ratios were unmeasurable. The remaining 7 p.A53T mutation carriers had significantly lower left caudate nucleus binding ratio ($p=0,01$), and a similar trend for the right caudate, compared to sPD patients. There was no difference in the putaminal binding ratios. The caudate / putamen signal ratio was significantly lower bilaterally in the p.A53T cohort (Right side $p=0,028$, Left side $p=0,018$). A similar degree of striatal asymmetry was observed in both the p.A53T and sPD subgroups. **Conclusions:** PD patients harboring the p.A53T SNCA mutation show evidence of a more severe, albeit variable, dopaminergic nigrostriatal denervation, mainly involving the caudate nucleus. This finding possibly reflects a more rapid disease progression, as well as a differential topography of nigrostriatal degeneration in the mutation carriers compared to sPD. This study was funded by the Michael J. Fox Foundation (PPMI study).

Morbus Hercules. The role of heracles in epileptology and Greek and Scythian mythology

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The word "epilepsy" is derived from Ancient Greek "επιληψις" (a seizure) which comes from "ἐπιλαμβάνειν" – "to seize, possess or afflict". In medical tractate "On the Sacred Disease" Hippocrates (c.460 – c.370 BC) gave the earliest available biological interpretation of the nature of epileptic process as brain disturbance. Epilepsy was also known by Greek and Latin physicians as "morbus Hercules" because Heracles (Hercules) was one of the most famous epileptic patients. Epilepsy caused a severe tragedy in life of Hercules - in the condition of complex partial seizure he killed his wife, two sons and also two children of his half maternal twin brother Iphicles. To expiate the crime, Heracles was required to carry out ten labors by the order of his cousin – Eurystheus, basileus of Argolid. During his life Heracles periodically had complex partial and secondary generalized seizures that were explained in Greek mythology as a penalization from the goddess Hera out of jealousy and revenge to the illegitimate son of her unfaithful husband - god Zeus. Episodes of rage, fury and crazy behavior of Hercules in the state of altered consciousness, accompanied by hyperemia, ophthalmic phenomena, hypersalivation with expired foam from mouth, chaotic automatisms, destroying everything and everyone, was noted in a number of legends and written sources, including the Euripides` drama "Madness of Heracles". Heracles is famous for his polygamy and fertility, and a lot of dynasties and tribes proclaimed Heracles as forefather. During his journey Heracles met in the cave the beautiful snake-woman Echidna, who bore him three sons, whose name was Agaphirs, Gaelon and Skyth - the ancestor of the Scythians. Famous Russian poets of "silver age" symbolists stile at the beginning of XX century - Alexander Block suffered from epilepsy and Valery Bryusov suffered from nightmares used antic legends, Heraclius and epileptic motives in their creativity.

Brain and mind: who is the puppet and who the puppeteer?

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The question in the title has fundamental social and legal implications. If the mind controls the brain, then there is FREE WILL and its corollaries, responsibility and dignity. If the brain controls the mind then there can be no FREE WILL because we cannot influence the brain connections and neurotransmitters that make the decisions for us. Hippocrates expressed what is taught in neuroscience today. "Men ought to know that from the brain, and from the brain only, arise our pleasures, joys, laughter and jests, as well as our sorrows, pain, griefs and tears." Neuroscience, considers the mind to be the activity of the brain (Hebb, 1949) and believes there is no ghostly substance inside us. Consistent with this, psychology abandoned the concept "soul" in the 1930s. Behavior is the outcome of two influences: genetic endowment and environment — nature and nurture. As Praxiteles sculpted Hermes out of a block of marble, so experience sculpts our character from the genetic material we are granted. Importantly, we have no choice of parents or the society we are born in. If only we could abandon our undesirable desires, our depression, our obsessions, our compulsions, our unrequited love. If only we were the authors of our thoughts and not merely observers of what the brain presents us. If only we could get hold of one of the strings with which our brain makes us dance. It seems the puppet is free only in as much as it loves its strings (Harris, 2012).

Epilepsy - then and now

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Hippocrates (460-370 BC) is called the father of medicine, founding the Hippocratic school. They were convinced that the brain is the source of all emotions and knowledge, although the ancient greek view differs from the present.

One of the most studied was the epilepsy, due to the spectacular aspect of the crisis.

In his book - 'On the Sacred disease', Hippocrate rises some theories, revolutionary from his predecessors, but quite far from the present view. Ul. The origin: hereditary , in the uterus a lack of 'purification' appears, conducting to a 'phlegmatic' person, as his parents. But, this may be depurated in childhood by skin eruptions. If not, the person becomes epileptic . They present with curved spine or mental retard. The clinic is well documented. The determinant factors: changing in temperature – cold , emotions. It may affect the lung or heart- the choking and hypersalivation or the bowel – spontaneous diarrhea. It presents on several forms: left seizures / right / both. Physiopathlogy: it is a defluxion of cold phlegma into the cava veine, that makes a blockage in the blood and inspiration and determines the hypersalivation, abnormal breathing and movement, loss of conscios, intellect. Prognostic is reserved for children and the elderly, as the young may heat the phlegma /ulAlthough the psysiopathology is far from the truth, the Hippocratic theories closely analysed may be interpreted in ways that modern medicine confirmed, increasing the value of logic observation, taking in consideration that the Corpus didn't make dissections on humans.

Sleep): A single-sensor automatic sleep-stage classification based on cross-frequency coupling

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Clinical specialists of sleep often score manually the sleep stages by visually inspecting the characteristic waveforms of a patient's neurophysiological signals like electroencephalogram (EEG), electrooculogram (EOG), electrocardiogram (ECG) and electromyogram (EMG). The whole approach of sleep scoring the neurophysiological recordings of a patient last over eight hours is a very demanding, difficult and time consuming procedure. Complementary, the limitations of manual sleep stage scoring have forced the scientists to develop techniques based on signal processing and machine learning for a completely Automatic Sleep Stage Classification (ASSC). Our first aim was to propose a novel EEG single-sensor ASSC based on dynamic reconfiguration of cross-frequency coupling (CFC) estimates using three different algorithms for the estimation of phase-to-amplitude coupling (PAC). The dynamic PAC (dPAC) was estimated between predefined frequency pairs applied to 10 s epoch lengths. We attempted to predict sleep stages (non-REM:N1,N2,N3,N4 ,REM:R) and wake (W) condition simultaneously as a six-class classification problem applied to 10 s epoch lengths. The proposed analytic scheme was demonstrated using the PhysioNet Sleep European Data Format (EDF) Database using sleep recordings from 41 subjects. The presented methodology achieved an absolute classification sensitivity, specificity and accuracy of $90.3 \pm 4.1\%$, $94.2 \pm 4.1\%$, and $94.6 \pm 4.2\%$., respectively, when multi-class Bayes Naive classifier is applied. Finally, our novel method was compared with those in recently published studies, enhancing further the high classification accuracy performance presented here.

An update on neuroradiology of traumatic brain injury: The Isu approach

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Patients with traumatic brain injury complain of symptoms like headaches, insomnia, depression, memory loss, bursts of anger, difficult in planning, bad social relationship, loss of some praxias. We present our magnetic resonance protocol, capable to explain those symptoms and provide a better diagnosis and prognosis for these patients as well as some examples from our daily routine. Material and methods: We have a standard protocol for patients suspected to have traumatic brain injury. The sequences are 3D T1-SPGR(BRAVO), 3D FLAIR, 3D susceptibility sequence (SWAN), Tensor, magnetic resonance spectroscopy with ROIs in frontal lobe and cingulate gyrus and resting state functional magnetic resonance. The subjects are 30 patients consulting for litigation, diagnosed with post-traumatic syndrome, no less than one year after trauma. 16 men and 14 women. Mean age: 38 yo (10yo-67 yo). Results: Susceptibility sequence was positive in 37% of patients. Cortical thinning was present in all patients in a following distribution: orbitofrontal cortex 90%, dorsal medial frontal cortex 83%, occipitaltemporal cortex 70%, central cortex 50%, hippocampus 26.7%, temporal cortex 23%, parietal cortex 20%. Fractional anisotropy was decreased in cingulum 57%, genu of the corpus callosum 50%, uncinated fasciculus 43%, splenium and inferior longitudinal fasciculus 23% each, superior longitudinal fasciculus 13%. Increased fractional anisotropy was present in cingulum 20%, superior longitudinal fasciculus 17%, splenium of the corpus callosum 13%, uncinated fasciculus and inferior longitudinal fasciculus 7% each. Magnetic resonance spectroscopy was abnormal in the frontal lobes (decreased NAA) in 73% and in posterior cingulate cortex in 28%. Abnormal connectivity in resting state fMRI was found in anterior cingulum 75%, posterior cingulum 67%, hippocampus 42% , insula 37%, caudate 25%, thalamus and prefrontal cortex in 13% each. Midbrain abnormal connectivity (13%) was always present in patients with persistent headache. Conclusion: Abnormal findings in our protocol matched neuropsychological examination and explained the symptomatology in patients with normal computed tomography and standard magnetic resonance. The symptoms, started after traumatic brain injury, correlated well in these patients

Utility of anatomic mri and specific neurological assessments in mild tbi

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Objective: This study investigated the utility of specific assessments and findings on high resolution anatomic MRI to evaluate Mild Traumatic Brain Injury (mTBI). **Background:** 3-word recall is commonly employed in patients with mTBI to assess memory function (Folstein et al., 1975). This test is usually normal and is probably inadequate for assessing these patients. 5-word recall, BESS, and Digits Backward are incorporated into the SCAT 2 (McCrary et al., 2009), but research has not demonstrated their effectiveness as longitudinal assessments (McCrea et al., 2013). The extent of incidental MRI findings in mTBI patients also remains unclear. **Methods:** 86 patients (15-50 years old), enrolled in the study either within 72 hours or 6-10 days of head injury, were followed over 3 months. Patients completed a maximum of 4 encounters which included a clinical exam, neurological assessments, and a multi-modal MRI at each visit. Chi-square and linear mixed models were used to longitudinally assess clinical symptoms found in the SCAT2. **Results:** Three longitudinal neurological assessments provided statistically significant results. The success rate of three trials of 5-Word recall increased from 14.1 correct out of 15 at Encounter 1 (E1) to 14.9 at Encounter 4 (E4) ($p=0.001$). Only the Single-Leg test of the Modified BESS was significant, dropping from an average of 4.1 errors at E1 to 1.8 at E4 ($p=0.001$). Subjects demonstrated a significant increase in successful 5-Digit Backward Recall (57.5% at E1 to 71.7% at E4; $p=0.043$). Anatomic MRI also provided interesting data; 20 of the 81 subjects imaged had stable white matter changes across encounters (24.7%) and 23 had incidental findings (28.4%). **Conclusion:** Neurologists may consider 5-Digits Backward, Single-Leg Balance, and 5-Word Recall tests over traditional 3-Word Recall, Gait/Romberg, and full BESS testing when assessing progression of mTBI patients over multiple visits. Incidental findings and white matter changes may be more prevalent in patients with mTBI compared to the normal population (Katzman et al., 1999, Hopkins et al., 2006).

Sleep disorders after traumatic brain injuries in amateur sports

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Introduction-Sleep disorders and other related problems are common situations after traumatic brain injuries Aim-Aim of this study was to evaluate such disorders Material-We evaluate 20 amateur sportsmen(range 18 to 38) , after traumatic brain injuries, during amateur sports activity. The specific sports activity was -soccer in 5 cases-25%- -basket ball in 3 cases-15%- -volley ball in 3 cases-15%- -hand ball in one case-5%- -tennis in one case-5%- -running in one case-5%- -beach volley ball in one case-%_ - boxe in one case-5%- -karate in one case-5%- -taekwondo in one case-5%- -wrestling in 2 cases-10%_ Methods'-A relation between sleep disorders and other related problems with 1)headache 2) dizziness 3) psychiatric symptoms was performed . Results-19 sportsmen were retrospectively considered (95%) .The most common types of injuries were falls ,10,52,6%. There is also a correlation between sleep disorders and other related problems (headache , dizziness , psychiatric symptoms) . Neurologic and psychiatric evaluation was very usefull such as appropriate medication in all 19,100%,cases Conclusions-We need more cases but that cognitive-accurate therapy and medication could be helpful in these situations. Sleep disorders after traumatic brain injuries are conditions that needs accurate evaluation and approach.

Sleep disorders after traumatic brain injuries in elderly people

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Introduction-Sleep disorders and other related problems are common situations after traumatic brain injuries in elderly people (65 years old) Aim-Aim of this study was to evaluate such disorders (65 years old) Material-We evaluate 20 elderly male people (range 65 to 75) , after traumatic brain injuries. Methods'-A relation between sleep disorders and other related problems with 1)headache 2) dizziness 3) psychiatric symptoms was performed . Results-19 elderly men were retrospectively considered (95%) .The most common types of injuries were falls ,10,52,6%. The second common type of injury was road traffic accident, 5 ,26,3%. The third common type of injury was domestic injuries, 4, 21,1% . There is also a correlation between sleep disorders and other related problems (headache , dizziness , psychiatric symptoms) . Neurologic and psychiatric evaluation was very usefull such as appropriate medication in all 19,100%,cases Conclusions-We need more cases but that cognitive-accurate therapy and medication could be helpful in these situations. Sleep disorders after traumatic brain injuries are conditions that needs accurate evaluation and approach.

Molecular mechanisms of postinjury axonal regeneration in primate retinal ganglion cells

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Purpose: To examine molecular mechanisms which are involved in regeneration of primate retinal ganglion cell axons in the monkey-human paradigm. **Methods:** Retinas were obtained from newborn to adult monkeys (*Callithrix jacchus*) immediately after death, freed from surrounding tissue and used to prepare explants which were cultured *in vitro*. Growth of axons was monitored using phase contrast microscopy and time-lapse video cinematography. Immunohistochemistry, Western blotting, qRT-PCR, proteomics and genomics were performed to characterize molecules associated with axonal growth. Then, siRNA experiments were conducted to identify the causal involvement of selected molecules in triggering axonal growth. **Results:** Primate retinal ganglion cells (RGCs) are known to lose the ability to regenerate cut axons during postnatal maturation, but the underlying molecular mechanisms are unknown. We screened for regulated genes in monkey RGCs during axon growth in retinal explants obtained from eye cadavers on the day of birth from New World marmosets (*Callithrix jacchus*), and hybridized the regeneration-related mRNA with cross-reacting cDNA on human microarrays. Neuron-specific human ribonucleoprotein N (snRPN) was found to be a potential regulator of impaired axonal regeneration during neuronal maturation in these animals. In particular, up-regulation of snRPN was observed during retinal maturation, coinciding with a decline in regenerative ability. Axon regeneration was reactivated in snRPN-knockout adult monkey retinal explants. These results suggest that coordinated snRPN-driven activities within the neuron-specific ribonucleoprotein complex regulate the regenerative ability of RGCs in primates, thereby highlight a potential new role for snRPN within neurons and the possibility of novel postinjury therapies. **Conclusions:** The data show that even after postnatal maturation, the molecular mechanisms for postinjury axonal growth are still existing, and can be reactivated to result in growth cone formation and lengthy axon extension. Understanding of the molecular mechanisms of axonal regeneration will help to develop therapeutic concepts for brain injuries.