Multiple sclerosis 2

P2709
The N400 component of event-related potentials in multiple sclerosis

V. Milosevic, S. Djuric, M. Jolic, M. Lazarevic
Clinic of Neurology, Clinical Center Nis, Serbia

Event related potentials (ERP) could be used in the study of cognitive impairment in multiple sclerosis. The N400 ERP component is considered to be an indicator of semantic memory access. The aim of the present study is to test the influence of lexical semantics on the N400 evoked potential component amplitude in multiple sclerosis patients and healthy subjects. The sample consists of 15 healthy subjects and 15 multiple sclerosis patients. The subjects were visually presented with word pairs lasting 1000ms (ISI 1000ms), of which the first word was representative of a semantic category (an animal or an inanimate object) and the second word was a concept that was either congruent or incongruent with the previously presented category. Evoked potentials were obtained by averaging 104 responses registered with the digital EEG system, where 16 electrodes were placed according to the 10-20 international system. Reference electrodes were located on mastoid processes (impedance<5kOhm, Hi-pass 0.1Hz, Low-pass filter 30Hz). A statistically significant difference in the amplitude of N400 effect was registered between the multiple sclerosis and healthy group in the interval ranging from 250 to 500ms after the stimulation (p<0.05). We have also registered a statistically significant (p<0.05) difference in N400 peak latency between the two studied groups. Evoked potentials could be a marker of a deficit in semantic memory access in multiple sclerosis.

P2710
The relation between helicobacter pylori infection and multiple sclerosis in Iranian patients

N. Mohebi1, M. Aghaei1, M. Mamarabadi1, M. Moghaddasi2
1Neurology, Tehran University of Medical Sciences, 2Iranian Centre of Neurological Researches (ICNR), Tehran, Iran

Background and aim: Multiple sclerosis (MS) is the most prevalent demyelinating disease in the central nervous system. There are known risk factors for MS. However, there is uncertainty in protective factors. Few studies have demonstrated that some chronic infections may have protective effects on this disease. This study was designed to investigate the relation between helicobacter pylori (HP) infection and prevalence and severity of MS patients.

Methods: In this case-control study, 163 MS patients and 150 sex- and age-matched controls were included. Blood samples for IgG and IgM anti-HP antibodies were collected from all individuals. Also Expanded Disability Status Scale (EDSS) was evaluated for MS patients. Suitable statistical analysis was used.

Results: Significant difference was seen in seropositivity between these two groups. (p<0.001) but no significant difference was seen in seropositivity between conventional and optico-spinal MS (p=0.522). No significant difference was seen in seropositivity among ages (p=0.075) and between genders (p=0.204). Significant difference was seen in EDSS value between seropositive and seronegative patients (p=0.017).

Conclusion: We concluded that patients with HP infection had lower incidence of multiple sclerosis, and MS patients with HP infection showed lower neurologic complications, which can demonstrate that HP infection may have protective influence on MS pathogenesis.
P2711

Antibodies against gangliosides in the serum of patients suffering from multiple sclerosis compared with healthy individuals

E. Koutsouraki, E. Hatzifilippou, T. Kalatha, A. Fotakidou, A. Kirytopoulos, S. Balyannis
1st Department of Neurology, Aristotle University, AHEPA Hospital, Thessaloníki, Greece

Multiple sclerosis (MS) is the most common demyelinating disease of the central nervous system. The mechanism of de- and re-myelination is still not extensively known. Gangliosides are a family of sialic-acid containing glycosphingolipids and they are highly concentrated in the nervous tissues. Increasing evidence suggests that gangliosides act as important mediators in both de- and re-myelination. We anticipate that the gangliosides could have both devastating and protective effects in respect to myelin. The aim of the present study was to correlate the levels of IgM antibodies against GM1, GD1b and GQ1b in the sera of MS patients with healthy individuals. We examined 56 patients suffering from definite multiple sclerosis, according to McDonald et al. diagnostic criteria, 16 men and 40 women, with a male to female ratio of 1:2.5, at a mean age of 39.1±1.58 years for women and 39.2±3.32 years for men, demonstrating 52% relapsing/remitting type, 43% secondary progressive and 5% primary progressive type of the disease, treated mainly with interferon-β (47%) and 44 healthy individuals (26 females and 18 males) with a mean age of 39.1±1.54 years for women and 39.8±2.26 years for men. None of the healthy controls demonstrated positive concentrations of anti-ganglioside antibodies. There was a statistically important difference (p<0.05) between controls and MS patients referring to anti-GM1 (75% positive MS patients) and anti-GD1b (57% positive MS patients) IgM antibodies while there were only 29% positive anti-GQ1b MS patients. Our findings indicate a possible role of anti-GM1 and GD1b antibodies in the pathogenesis of MS.

P2712

Bioequivalence of BG-12 administered as a single 240 mg capsule and two 120mg capsules: findings from a randomized, two-period crossover study

S.I. Sheikh1, I. Nestorov1, R. Manchanda1, D. Goldman1, J. O’Gorman1, H. Russell2, M.A. Matson3, M. Tighe1, K.T. Dawson1
1Biogen Idec Inc, Weston, 2PROMETRIKA, LLC, Cambridge, MA, 3Prism Research, St Paul, MN, USA

Introduction: Phase 3 trials demonstrated significant efficacy of BG-12 (dimethyl fumarate [DMF]) 240mg (administered as two 120mg capsules) twice or three times daily for treatment of relapsing-remitting multiple sclerosis. Bioequivalence between BG-12 administered as two 120mg capsules and a single, same-size, 240mg capsule was assessed in healthy volunteers.

Methods: In this randomized, open-label, two-period crossover bioequivalence study, subjects received two 120mg capsules or a single 240mg capsule of BG-12 following overnight fast. Blood samples were drawn 15 minutes pre-dose and serially at twelve time points from 30 minutes to 12 hours post-dose for determination of pharmacokinetic (PK) parameters for monomethyl fumarate (MMF), the main metabolite of DMF.

Results: 81 subjects were enrolled in the study; 77 completed both treatment periods. Concentration-time profiles were very similar following dosing with two 120mg capsules or a single 240mg capsule of BG-12 following overnight fast. Blood samples were drawn 15 minutes pre-dose and serially at twelve time points from 30 minutes to 12 hours post-dose for determination of pharmacokinetic (PK) parameters for monomethyl fumarate (MMF), the main metabolite of DMF. Bioequivalence between formulations was established per standard regulatory criteria. BG-12 was well tolerated. Safety profiles for both formulations were consistent with those seen in previous healthy volunteer studies of BG-12.

Conclusions: Single-capsule administration of BG-12 240mg demonstrated bioequivalence with an equivalent dosage administered as two capsules. Administering the 240mg dose in a single capsule would halve the number of capsules required to take BG-12, which coupled with acceptable tolerability, has potential to promote treatment adherence.

Supported by: Biogen Idec Inc.
P2713

**HLA-DRB1*1501 intensifies the impact of IL-6 promoter polymorphism on the susceptibility to multiple sclerosis in an Iranian population**

M. Shahbazi, D. Roshandel, H. Ebadi, D. Fathi, M. Zamani, A. Tahmasbifar, S. Shahbazi

1Medical Cellular Research Center, Golestan University of Medical Sciences, 2Golestan University of Medical Sciences, 3Tehran University of Medical Sciences, Gorgan, Iran

**Background:** The multifunctional cytokine interleukin-6 (IL-6) is involved in inflammatory processes in the central nervous system. It is well documented that the amount of IL-6 is increased in serum, cerebrospinal fluid and central nervous system lesions of patients with multiple sclerosis. A single nucleotide polymorphism at position -174 in the IL-6 gene promoter appears to influence IL-6 expression. Recently, several researchers have focused on HLA-DR alleles, specifically HLA-DRB1*1501, as a potential risk allele in the pathogenesis of multiple sclerosis.

**Method:** Genomic DNA was extracted from whole blood of 345 patients with multiple sclerosis and 426 control subjects. The SSP-PCR method was used to determine genotypes and Fisher's exact test was applied to determine differences between groups.

**Results:** A-DRB1*1501 was observed more frequently among multiple sclerosis patients compared with healthy subjects (45% and 34%, respectively; OR=1.6, 95% CI=1.2-2.2, \( p=0.0018 \)). At the IL-6/-174 position, the G allele had higher frequency among multiple sclerosis patients compared with controls (77% and 70%, respectively; OR=1.4, 95% CI=1.1-1.8, \( p=0.0038 \)). This difference was more significant among HLA-DRB1*1501-positive patients and controls (81% and 67%, respectively; OR=1.9, 95% CI=1.5-2.5, \( p<0.0001 \)).

**Discussion:** Our results have shown that the G allele at the IL-6/-174 promoter polymorphism may be associated with development of multiple sclerosis in this population, and may be strengthened by HLA-DRB1*1501.

**Conclusions:** We suggest more studies to confirm these results in other populations.

---

P2714

**Incidence of multiple sclerosis in the Sarajevo region during a 25-year period**

J. Djelilovic-Vranic, A. Alajbegovic, M. Tiric-Campara

Neurology Clinic, Clinical Center of Sarajevo University, Sarajevo, Bosnia-Herzegovina

**Introduction:** Multiple sclerosis as auto-immune disease has a tendency of increase in the incidence and total prevalence in the world, especially in some areas.

**Goal:** To determine the incidence of multiple sclerosis in the Sarajevo region during a 25-years period.

**Material and methods:** We analysed all new cases of MS, during the 25-year period (January 1986-December 2010) in the Sarajevo region, who were treated at the Neurology Clinic. All patients along with medical history and neurologic findings, underwent cerebrospinal fluid examination, MRI of the brain and spinal cord and EP, and were followed in order to confirm the MS diagnosis.

**Results:** In the first five years (1986-1990), there were 45 newly diagnosed cases of MS (29F and 16M). During the war in Bosnia (1991-end-1995), there were only 27 newly discovered MS cases (19F and 8M), and in the period from 1996 to end of 2000 there were 124 new MS cases (89F and 35M). Finally in the years 2001 until end of 2010 the number of new MS cases was higher each year. In the period 2001 until the end of 2005, there were 152 new MS cases (113F and 39M), and from 2006 until the end of 2010, 169 new cases (123F and 46M) with age from 12-57 years.

**Conclusion:** Multiple sclerosis in the region of Sarajevo during a 25-year period, showed an increase in the incidence and prevalence and by Kurtzke scale classifies the region into a zone of higher risk of MS.
P2715
Poor sleep in patients with multiple sclerosis

H.M. Lunde¹, T. Aae², W. Indrevåg², J. Aarseth¹, K.-M. Myhr¹, B. Bjorvatn¹, L. Bo¹
¹The Norwegian Multiple Sclerosis Competence Centre for MS, Department of Neurology, Haukeland University Hospital, ²The Norwegian Multiple Sclerosis Competence Centre for MS, University of Bergen, Faculty of Medicine and Dentistry, ³National Competence Centre of Sleep Disorders, Haukeland University Hospital, Bergen, Norway

Introduction: Poor sleep quality is prevalent among patients with multiple sclerosis (MS). Specific sleep disorders, MS-related symptoms and socio-demographic factors can impair sleep in these patients. We studied the influence of socio-demographic and clinical factors on sleep quality in MS. This study was performed to survey causes and prevalence of poor sleep in MS.

Methods: A total of 90 patients with MS and 108 sex- and age- matched controls participated in the study. Sleep quality, daytime sleepiness and symptoms of pain, fatigue and depression were registered by use of questionnaires. Results were compared between patients and controls and among good and poor sleepers in the patient group.

Results: Poor sleep was reported in 67.1% of MS patients compared to 43.9% of controls. Use of antidepressant medication, depression, pain and fatigue were more frequent in patients. Factors associated with poor sleep in the study population were fatigue, pain and MS. In MS patients, these factors were more prevalent in female gender, when using immunomodulatory drugs and in increased psychological impairment of MS (MSIS-29).

Conclusion: Poor sleep in MS patients was common, and more frequently reported in females, patients on immunomodulatory drugs and in patients with psychological impairment. Improved sleep may be achieved in MS-patients through early identification and treatment of modifiable risk factors for poor sleep.

P2716
White matter microstructural alteration in multiple sclerosis

E. Tóth, Z.T. Kincses, N. Szabó, K. Bencsik, L. Vécsei, Neuroimaging Research Group Neurology Department, University of Szeged, Szeged, Hungary

Introduction: White matter T2 hyperintense lesions are the diagnostic cornerstones of multiple sclerosis (MS). Alterations of the normal appearing white matter (NAWM) are also known. Diffusion weighted imaging (DWI) can reveal the integrity of white matter tracts and provide information about the underlying microstructure.

Methods: DWI data, with 60 diffusion directions were acquired in 31 relapsing-remitting MS patients and 31 age- matched, healthy controls. Lesions were manually identified on FLAIR images. Diffusion parameters such as fractional anisotropy (FA), mean (MD), axial (AD) and radial diffusivity (RD) were compared between patients and controls along a white matter skeleton, representing the core of fibre bundles. Voxel-wise correlations with EDSS, lesion load (LL) were also calculated.

Results: We found decreased FA (p<0.0002) in all the white matter fibre bundles in regions, where lesions were found and in NAWM. In similar regions, MD and RD were increased indicating demyelination predominantly. The increase of AD was only found in central fibres and in intrathalamic white matter, where FA was not reduced. In MS patients EDSS showed negative correlation with FA (p<0.035) and positive with RD (p<0.032) in the corpus callosum. In some periventricular locations only negative correlations with FA were found. LL showed a negative correlation with FA in all major fibre bundles (p<0.001), and positive correlations with AD, RD and MD in the thalami.

Conclusion: These results call attention to the regionally specific microstructural alterations in MS in the lesioned as well as in the NAWM.
**P2717**

**Stabilometry as a potential method of measuring the progression rate of relapsing-remitting multiple sclerosis (RRMS)**

N. Spirin, D. Kasatkin, A. Serednichuk  
Yaroslavl State Medical Academy, Yaroslavl, Russia

**Background and objectives:** The maintenance of vertical posture in humans is one of the most important functions. High speed and frequency of the external forces acting on the postural balance, determine the need for accurate and rapid interaction between the prefrontal cortex and cerebellum, as well as a complex sensory systems. Broad representation in the cerebral white matter tracts and high sensitivity to a decrease in the rate of interest on them determines the characteristics of the study to maintain equilibrium in the focal and diffuse white matter pathology of the cerebral hemispheres, particularly in the RCF.

**Materials and methods:** 70 patients (22 men and 48 women), RRMS, remission, age 21-55 years, with disease duration of 0.6 to 15 years; EDSS, stabilometry (European position), rate of deviation of center of pressure (Voe and Vce). Statistical analysis - non-parametric statistic: R Spearman, U Mann-Whitney.

**Results and conclusion:** Voe and Vce increases with the duration of disease (R=0.52, p<0.001 and R=0.52, p<0.001) and the rate of EDSS (R=0.36, p=0.001 and R=0.31, p=0.008). Groups with and without an atactic exacerbation significantly differ in Soe and Sce (U=397.5, p=0.014 and U=426.0, p=0.034). Thus, the speed deviation of center of pressure related to disease duration and rate of EDSS and is not associated with clinical signs of relapse, therefore may be potential markers for determining the rate of growth of a neurodegenerative process.

**P2718**

**PEGylated interferon beta-1a: meeting an unmet medical need in the treatment of relapsing multiple sclerosis**

B. Sperling  
Biogen Idec Inc., Weston, MA, USA

**Objective:** Review the rationale for and clinical development of PEGylated interferon beta-1a (PEG-IFN beta-1a).

**Background:** PEG-IFN beta-1a is being developed as a multiple sclerosis (MS) treatment option that is at least as safe and effective as current platform therapies, but with improved convenience.

**Methods:** A phase 1a single-dose (SD) study comparing PEG-IFN beta-1a (63-188 mg) with intramuscular (IM) IFN beta-1a (30 mg) and a phase 1b multiple-dose (MD) study comparing subcutaneous (SC) PEG-IFN beta-1a (125mg) every 2 or 4 weeks with placebo were conducted in healthy volunteers. An on-going, global, randomized, double-blind, placebo-controlled phase 3 study (ADVANCE) is evaluating the efficacy, safety, and tolerability of 125µg SC PEG-IFN beta-1a.

**Results:** SC or IM administration of SD PEG-IFN beta-1a produced 4-fold higher exposure and 2-fold longer half-life than IM-IFN beta-1a at doses with equivalent in vitro potency. Pharmacokinetics of PEG-IFN beta-1a were similar for IM and SC administration, and exposure was dose-proportional. PEG-IFN beta-1a dosed every 2 or 4 weeks did not cause drug accumulation; pharmacokinetic profiles resembled those in the SD study. Serum neopterin levels peaked at 72 hours post-dose, returning to baseline approximately 10 days post-dose. PEG-IFN beta-1a had similar safety and tolerability as IM IFN beta-1a in phase 1 studies. ADVANCE has commenced at 227 sites in 26 countries, with 1516 patients randomized.

**Conclusions:** PEG-IFN beta-1a is safe and well-tolerated and exhibits greater exposure and activity than IM-IFN beta-1a. It has the potential to become a safe, efficacious, and convenient MS treatment option.
P2719
Safety and efficacy of natalizumab (Tysabri) in older patients and/or with longer disease duration: a Swedish nationwide long term follow up study
H. Matell, O. Sveinsson, C. Holmén, J. Hillert, T. Olsson, F. Piehl
Karolinska Institute, Stockholm, Sweden
Introduction: In the pivotal study of natalizumab in monotherapy (AFFIRM) RRMS patients aged 18-50y with EDSS 0-5 were eligible. The safety and efficacy of natalizumab in older patients and/or in more advanced disease is not known.
Methods: Since 2006 a post-marketing surveillance study in Sweden (IMSE) monitors long-term effectiveness and adverse events of natalizumab. Patients are followed in a web-based MS registry. As of 2/29/2012 1740 patients have been included (71.4% women). 1412 patients (81.1%) were diagnosed with RRMS and 95 (5.5%) with SPMS. 214 patients were >50y of age.
Results: As expected, older patients (>50y) had a higher starting EDSS and lower SDMT score than younger patients. However, the degree of improvement did not differ significantly between the groups. SDMT increased from 43.9 to 49.1 (>50y) and from 49.4 to 57.1 (<50y) over 24 months. Also the safety profile was similar in both groups. 5 cases of progressive multifocal leukoencephalopathy were reported, all aged <50y. However, older patients and patients with higher EDSS scores were more likely to interrupt treatment due to “lack of effect” or “SPMS”, suggesting that natalizumab is less effective in more advanced disease states. In an on-going analysis these data are validated against clinical records for a cohort of 400 patients followed at the Karolinska University Hospital in order to characterize clinical, neuroradiological and biomarker factors associated with beneficial natalizumab treatment outcomes.
Conclusion: Natalizumab is safe also in older patients, however, older patients are more likely to interrupt treatment due to an insufficient effect.

P2720
The functional system involvement of a first multiple sclerosis attack influences the location of subsequent relapses
D. Vecchio1,2, E. Tsantes1, S. Ruggerone2, C. Senesi3, I. Lucenti2, E. Curti3, R. Cantello1,2, F. Granella3
1Neurological Clinic, University of Piemonte Orientale, 2Multiple Sclerosis Center, "Maggiore della Carità" Hospital, Novara, 3Multiple Sclerosis Center, Department of Neurosciences, University of Parma, Italy
Objective: To determine the risk of repeating the involvement of the same Functional System (FS) after a first demyelinating clinical attack in a cohort of patients with relapsing-remitting multiple sclerosis (RRMS).
Methods: We identified patients at disease onset, presenting at least two attacks, consecutively referred to two Italian MS Centres. We collected Kurtzke FS involvement in all the attacks.
Results: We enrolled 187 patients (127 female) with two attacks, 117 had three relapses. 108 patients (57.8%) presented in the second attack at least one FS involved in the first, 68 (58.1%) repeated in the third one FS previously involved. The risk of repeating the same FS in the first and second attack was higher for cerebellar (OR 9.1, 95% CL 2.0-41.7; kappa 0.26, -95% CL 0.02-0.51), followed by brainstem (3.5, 1.6-7.4; 0.24, 0.08-0.40), visual (3.8, 1.8-8.0; 0.27, 0.12-0.43), motor (3.1, 1.5-5.9; 0.26, 0.11-0.40), and sensitive (2.1, 1.2-3.8; 0.18, 0.04-0.33) involvements. Cerebellar (5.7, 1.0-34.6; 0.19, -0.10-0.49), visual (4.0, 1.5-10.6; 0.27, 0.07-0.47), and motor (2.7, 1.2-6.1; 0.22, 0.04-0.40) FS at the first attack, and visual (3.4, 1.5-7.8; 0.27, 0.09-0.45), and brainstem (2.8, 1.0-7.8; 0.18, -0.02-0.39) FS at the second represented at the third. Among patients repeating visual symptoms, 9 (56.3%) were affected in the same eye in the first and second attack, 6 (75.0%) in the second and third, and 2 (33.3%) in the first and third.
Conclusions: The involvement at first attack of a FS was predictive for its recurrence at the second and third relapses.
P2721

Imaging comparison study of multiple sclerosis (MS) and neuromyelitis optica (NMO)

J.-G. Liu¹, X.-K. Qi², K.-H. Zheng³, H.-L. Zhang²
¹Neurology, ²Navy General Hospital, ³Iconography, Navy General Hospital, Beijing, China

Objective: To compare imaging characteristics of MS and NMO for differential diagnosis.

Methods: The imaging characteristics of 60 MS and 48 NMO cases were retrospectively studied.

Results: The three top predilection sites of the brain in head MRI of MS were para-lateral ventricles (34/60), subcortex white matter (27/60), brain stem (23/60), and it also involved the cortex (9/60). By contrast, brain lesions were observed in 59.4% of NMO, and the three top predilection site of brain lesions in NMO were brain stem (13/32), circum-lateral ventricles (12/32), subcortex white matter (7/32), furthermore, the lesions surrounded the third ventricle (6/32) and the tegmentum of brain stem near periaqueduct (8/32) of NMO were not found in MS. The lesions of spinal cord shown in MRI of MS were typically oval, peripheral, and asymmetric, but in NMO longitudinally extensive and central conversely. The mean number of involved vertebral segments in NMO is higher than 3, and in MS less than 3.

Conclusions: Several distinct imaging characteristics between NMO and MS as follows: like MS, most patients with NMO may have brain lesions, but its distributions may be different from MS's, such as the lesions surrounding the third ventricle and the tegmentum of brain stem near periaqueduct of NMO. Compared with MS, the cortical lesions may be more rarely observed for NMO. The mean number of involved vertebral segments in NMO is higher than 3, and in MS less than 3.

P2722

Poor sleep is associated with low health related quality of life in multiple sclerosis patients

M. Vitkova¹,², J. Rosenberger², I. Nagyova², M. Chylova²,³, P. Mikula², J. Szilasióva¹, Z. Gdovinova³, J.P. van Dijk²,⁴, J.W. Groothoff⁴
¹Department of Neurology, P.J.Safarik University Kosice, ²Graduate School Kosice Institute for Society and Health, P.J.Safarik University Kosice, ³1st Department of Psychiatry, Faculty of Medicine, Safarik University, Košice, Slovak Republic, ⁴Department of Community & Occupational Health, University Medical Center Groningen, Groningen, The Netherlands

Introduction: Sleep disturbances in patients with multiple sclerosis (MS) can be associated with lower health related quality of life (HRQoL). The aim of study was to explore the association of poor sleep with HRQoL in MS patients and to explore the clinical and psychosocial factors related to poor sleep quality.

Methods: The study comprised 121 patients (78.5% women, mean age 40.2±9.7 years, mean EDSS 3.3±1.5). Sleep disturbances were measured by the Pittsburgh Sleep Quality Index (PSQI), fatigue by the Multidimensional Fatigue Inventory (MFI-20), anxiety and depression by the Hospital Anxiety and Depression Scale (HADS) and HRQoL by the Short Form 36 (SF-36). Functional disability was assessed using Expanded Disability Status Scale (EDSS). Multiple linear regression analyses were performed.

Results: The frequency of poor sleep was 48.9%. Patients with poorer sleep had worse score on Physical Component Summary (PCS). The model consisting of physical fatigue (p=0.001), EDSS (p=0.001) and poor sleep (p=0.03) explained 60% of variance in PCS. Sleep disturbances were not found to be associated with Mental Component Summary. Independent predictors of poorer sleep were depression (p=0.007) and general fatigue (p=0.02). This model explained 35% of the variance of the PSQI.

Conclusion: Poor sleep is associated with low physical HRQoL in MS patients. Depression and general fatigue were the main variables related to poor sleep. Thus, effective treatment of these conditions could improve quality of sleep and to increase a patient’s HRQoL.
P2723

Advances in MS patient management: update of Multiple Sclerosis Documentation System ‘MSDS 3D’

R. Kempcke, T. Schultheiß, T. Ziemssen
Multiple Sclerosis Centre at the Department of Neurology, Technical University Dresden, Germany

Development and evaluation of the new Multiple Sclerosis management and documentation tool MSDS 3D. There is an increasing spectrum of current immunomodulatory treatment options (e.g. Fingolimod, Natalizumab) requiring an inevitable demand for software-guided documentation and standardized patient management. Recently we presented the three-dimensional Multiple Sclerosis Documentation System “MSDS 3D” as an approach to integrate online data given by physicians, MS nurses and the patients. MSDS 3D allows documentation and visualization of visit schedules and mandatory examinations via defined modules on a touch-screen based interface. In a multi-centre based setting, 200 patients and nine treating neurologists assessed applicability of MSDS 3D in specialised Multiple Sclerosis outpatient departments. Study modules included touch-screen based tasks for physicians (patient history, EDSS, clinical global impression) and for patients (electronic questionnaires for fatigue, depression, disability). Management and documentation was evaluated as efficient by the majority (88%) of physicians. 8 of 9 neurologists considered MSDS 3D as future tool for patient documentation and management. 68% of patients preferred using the electronic questionnaire rather than the paper-based form. Management of touch-screen interface was appreciated as not stressful by almost all participants (87%). The majority of patients (83%) considered using electronic questionnaires in the future. The Multiple Sclerosis Documentation System MSDS 3D has successfully been improved and evaluated in a multi-centre setting. Additional tools with special regard to patient management have been implemented. It has been possible to combine information given by the patient with other MS relevant data. Acceptance by patients and treating neurologists has been high.

P2724

Tonic spasms in neuromyelitis optica

L. Elsone, T. Townsend, K. Mutch, K. Das, M. Boggild, A. Jacob
The Walton Centre NHS Foundation Trust, Liverpool, UK

Introduction: Tonic spasms (TS) are paroxysmal involuntary brief, stereotyped usually unilateral and often painful dystonic posturing of the limbs, usually due to spinal cord demyelination. 4% multiple sclerosis patients report TS.

Objective: To assess the characteristics of TS in patients with AQP4 antibody positive (AQP4 +) neuromyelitis optica (NMO) or NMO spectrum disorder patients (NMOSD) with transverse myelitis (TM).

Methods: Retrospective case note review followed by prospective telephone/clinic interviews of all the 46 AQP4+ patients who attended the National NMO clinic in Liverpool, UK after 1st Jan 2011.

Results: 44/ 46 patients had TM. 25/ 44 (57%) of these patients reported TS. Two patients with insufficient data were excluded and one patient refused consent. 22 patients were included in further analysis. TS developed within 1 month from onset of TM in 9 patients (40.1%) and within median 2 (0.5-8) months in 13 patients (59.9%). In a single case, TS was followed by sensori-motor symptoms of TM, 2 weeks later. In most cases (54.5%) TS occurred following/during first episode of TM. TS were painful in 63.6% and lasted a median for 40 (10-240) seconds with frequency one a day to one every ten minutes. TS corresponded to longitudinally extensive spinal cord lesion in 95.4%. Moderate or good response was seen in 9/12 patients (75%) who tried Carbamazepine.

Conclusions: TS is a very common (>60%) disabling residual symptom of transverse myelitis associated NMO and responds well to Carbamazepine. It can rarely precede an episode of transverse myelitis.
P2725
Frequency and distribution of autoreactive antibodies between multiple sclerosis and neuromyelitis optica in Japan
K. Takahashi1, K. Tanaka2
1Iou Hospital, 2Neurology, Kanazawa Medical University, Kanazawa, Japan

Background: Previous reports of multiple sclerosis (MS) with autoreactive autoantibodies might include cases of neuromyelitis optica (NMO), especially in Japan. This study investigated the frequency and distribution of autoreactive antibodies in MS and NMO.

Subjects: A total of 48 patients fulfilled the inclusion criteria for MS in 2010 and 2011 of those patients fulfilled the revised NMO criteria in 2006.

Results: The presence of 1 or more autoreactive antibodies was demonstrated in 41% of MS and 64% of NMO patients. Although Sjögren’s syndrome-associated auto-antibodies such as anti-SS-A/Ro antibodies and thyroiditis-associated auto-antibodies such as anti-thyroglobulin antibodies and anti-thyroid peroxidase antibodies were shown in both groups. Antinuclear antibodies, anti-Sm antibodies, anti-single stranded DNA antibodies and lupus anticoagulant (LAC) were only positive in MS, while PR3-ANCA was only found in NMO. No patient in either group had anti-RNP, anti-SS-B/La, antiphospholipid (aCL), aCL-beta2-glycoprotein I complex antibodies, anti-MPO-ANCA, Scl-70, or anti-centromere antibodies.

Discussion: The frequency of autoreactive antibodies was similar to that in previous reports, with the exception of aCL and LAC. No patient in either group had anti-RNP, anti-SS-B/La, anticardiolipin (aCL), aCL-beta2-glycoprotein I complex antibodies, anti-MPO-ANCA, Scl-70, or anti-centromere antibodies.

P2726
Cross-sectional study on relationship between Symbol Digit Modalities Test, plasma cerebrosterol concentration and MRI-based brain volumes of MS patients
G. Bergendal1, L. Stawiarz2, O. Almkvist1,3, S. Fredrikson2, A. Glaser2, J. Hillert2, T. Masterman2, I. Björkhem5, V. Leoni6, V.D. Karrenbauer2
1Department of Neurobiology, Care Sciences and Society, 2Department of Clinical Neuroscience, MS Research Group, Karolinska Institutet, 3Department of Psychology, Stockholm University, 4Department of Clinical Neuroscience, Division of Neurology, 5Department of Laboratory Medicine, Karolinska Institutet, Stockholm, Sweden, 6Laboratory of Clinical Pathology and Medical Genetics, Foundation IRCCS, Neurological Institute Carlo Besta, Milan, Italy

Introduction: Cerebrosterol (24S-hydroxycholesterol, 24OHC) is a brain-specific cholesterol elimination product that passes freely over the blood-brain barrier (1). 24OHC/cholesterol ratio in plasma was found to correlate positively with grey matter volume (GMV) and negatively with CSF volume in 33 slightly cognitively impaired individuals (1). Symbol Digit Modalities Test (SDMT) measures information processing speed and is a sensitive marker of cognitive dysfunction in MS patients (2). In MS cortical lesion load and cortical atrophy are associated with impaired cognitive function (3, 4).

Objectives: To investigate a possible relationship between plasma 24OHC concentration, cerebral dysfunction evaluated by SDMT and MRI-based atrophy measures in a cross-sectional sample of MS patients with subjective cognitive impairment (SCI).

Method: 24 MS patients with SCI were consecutively referred to a neuropsychologist at the MS centre. MRI scanning, SDMT examination and 24OHC measurement were performed once during the period 2004-2005. Volumetric analysis of brain tissues was performed by SIENAX, FSL software. Cerebrosterol concentrations were analysed by isotope dilution-mass spectrometry.

Results: We found positive correlation between SDMT value and GMV; negative correlation between SDMT and lateral ventricles’ CSF volume; negative correlation between SDMT value and 24OHC concentration; positive correlation between lateral ventricles’ CSF volume and 24OHC.

Conclusion: The negative correlation between SDMT value and 24OHC concentration in our MS sample is of interest in relation to a recent study by Hughes et al (5) who found that subjects with high plasma levels of 24OHC are more likely to develop cognitive impairment over 8 years of follow-up.
P2727

Chronic cerebrospinal venous insufficiency in patients with multiple sclerosis: a case-control study from Iran

M. Mehrpour1,2, M.R. Motamed1, M. Nabavi3, M.A. Sahraeian4

1Neurology, Firoozgar Clinical Research Development Center, Tehran University of Medical Sciences, 2Firoozgar Clinical Research Development Center (FCRDC), Tehran University of Medical Sciences (TUMS)- Firoozgar General Hospital, 3Neurology, Shahed University, 4Neurology, Tehran University of Medical Sciences- Sina Hospital, Tehran, Iran

Introduction: Chronic cerebrospinal venous insufficiency (CCSVI) is a newly suggested cause for multiple sclerosis (MS) detected by color-coded Doppler sonography. Our aim was to evaluate the relationship between CCSVI and MS compared to the control group.

Methods: The study was performed on 84 MS patients and 115 healthy subjects. The presence of at least two of the extra- and/or intra-cranial Zamboni’s criteria was considered positive for evidence of CCSVI.

Results: Although the total number of MS patients with any detectable CCSVI criterion was significantly higher than the controls (22.6% vs. 10.4%, p=0.019), only one out of 84 patients fulfilled the Zamboni’s criteria (1.2% vs. none, P=0.422).

Conclusion: Our results do not support the presence of a relationship between MS and CCSVI criteria defined by Zamboni.

P2728

Multiple sclerosis associated fatigue and sleep disturbances

M. Kiziria1, T. Vashadze1, D. Gugutsidze1, A. Chikadze2, L. Khuchua2, M. Jibladze2, A. Tsiskaridze1, R. Shakarishvili1

1Ivane Javakhishvili Tbilisi State University, 2Georgian Association of Electrophysiology and Sleep Medicine, Tbilisi, Georgia

Background: Fatigue is the most frequent symptom in MS patients. It is poorly understood and difficult to treat. Patients with MS do not often distinguish between fatigue and sleepiness. Excessive somnolence, inappropriate daytime sleep and sleep disorders are common in patients with MS.

Objective: To determine sleep disturbances associated with fatigue in patients with MS and correlation with the location of demyelinating lesions seen on MRI.

Materials and methods: 10 consecutive patients with RRMS who had fatigue based on fatigue questionnaire (MFIS) underwent nocturnal polysomnography. There were 3 men and 7 women aged between 20 and 32 with EDSS ranging between 2.0 and 4.5. 8 patients reported sleep-related problems. These included difficulties initiating sleep and/or frequent awakenings due to spasms in the legs (7), difficulties in initiating or maintaining sleep (4), snoring (2) and nocturia (3). All patients were screened for depression with Beck Depression Inventory and no one had scored more than 14.

Results: Of the 10 fatigue patients with MS all had REM sleep without atonia, 2 had REM-sleep associated motor activity in the legs, 7 had frequent awakenings and significantly reduced sleep efficiency, 5 had hypopnoea. One patient had sleep apnoea and fatigue was especially prominent in this case. 2 had snoring. All patients had MRI brain stem lesions and two of them had demyelinating lesions in the pons.

Conclusion: We have disclosed a relationship between fatigue-associated sleep abnormalities in MS patients and MRI brain stem lesions. These abnormalities may play a role in the pathophysiology of poorly understood MS fatigue.
P2729
Socio-economic factors in childhood and risk of multiple sclerosis
N.M. Nielsen¹, K.T. Jørgensen¹, P. Bager¹, E. Stenager²,³,⁴, B.V. Pedersen¹, H. Hjalgrim¹, N. Koch-Henriksen²,³, M. Frisch¹
¹Department of Epidemiology Research, Statens Serum Institut, ²The Danish Multiple Sclerosis Registry, Rigshospitalet, Copenhagen University Hospital, ³National Institute of Public Health, University of Southern Denmark, Copenhagen, ⁴Dept of Neurology, MS Clinic of Southern Jutland, Esbjerg, Denmark

Introduction: Findings concerning the possible link between socio-economic status (SES) in childhood and subsequent risk of multiple sclerosis (MS) have been ambiguous.

Methods: In a national cohort comprising 1.6 million Danes born 1966 to 1992, we studied the impact of childhood SES on the risk of MS between 1981 and 2007 using nation-wide information about household income and parental educational level (basic, secondary or higher) at the person’s 15th birthday. The association between childhood SES and risk of MS was evaluated by means of MS incidence rate ratios (RR) with 95% confidence intervals (CI) obtained in log-linear Poisson regression analyses with adjustment for potential confounders.

Results: Overall, we found no strong association between childhood SES and risk of MS. We did, however, observe a tendency towards a reduced risk of MS among children from higher-educated households, notably as judged from levels of maternal education. Children whose mothers had a secondary (RR=0.95 (95% CI; 0.86-1.04)) or higher (RR=0.86 (95% CI; 0.76-0.97)) level of education were at 5% and 14% reduced risk of MS, respectively, compared to children of mothers with basic educational level (trend test, p=0.02). Results were practically unchanged in an analysis restricted to persons aged 15 to 29 years, among whom the possible effect of personal SES on MS risk is likely to be limited.

Conclusion: In Denmark, SES in childhood seems not to be of major importance for the subsequent risk of MS. However, offspring of well-educated mothers may be at a slightly reduced risk of MS.

P2730
Effect of natalizumab therapy on cognitive function in patients with multiple sclerosis
S. Jónsdóttir¹,², H. Hjaltason¹,², S. Práínsdóttir¹,²
¹Neurology, Landspitali-The National University Hospital of Iceland, ²Faculty of Medicine-School of Health Sciences, University of Iceland, Reykjavik, Iceland

The objective of the study was to examine the effect of one-year therapy with natalizumab on cognitive function in patients with active relapsing-remitting multiple sclerosis (MS).

40 patients (17 males, 23 females; mean age 41.7 years; mean education 15.2 years) who received natalizumab therapy at the National University Hospital of Iceland from 2008 to 2011 participated in the study. To control for practice effects 20 healthy controls matched on age and sex were also included in the study. Neuropsychological tests measuring various domains of cognitive function were administered before natalizumab therapy started and again after one year of therapy. Same tests were administered to the control group with one year interval. Changes were assessed using the Wilcoxon test. A p value <0.05 was considered statistically significant.

The results show that before therapy MS-patients were impaired on all tests compared to controls. After one-year therapy with natalizumab performance had significantly improved on tests that measure verbal learning (p=0.00), delayed verbal memory (p=0.00), word retrieval (p=0.01), judgement of line orientation (p=0.03), psychomotor speed (p=0.01) and fine motor function in both hands (p=0.02 and 0.03). A trend was observed on a test measuring inhibition (p=0.09). Performance on other tests remained unchanged and did not worsen on any test. The performance of the control group remained unchanged on every test except one, where it improved.

After one year of therapy with natalizumab cognitive function in patients with MS had improved, especially in memory and executive function. Other aspects of cognitive function were maintained.
P2731

Walking Disability Index for multiple sclerosis patients

F.K. Mutluay, A. Siva

Introduction: Neurological evaluation of multiple sclerosis (MS) patients often involves the determination of heel, toe and tandem walking abilities, each assessed as pass or fail. A more graded approach to this scoring method, proposed in this study, permits rapid yet subtle scoring of walking disability.

Methods: Five step tandem, toe and heel walking abilities (no aid) of 348 MS patients were scored as: one (pass) if completed normally; ½ (partial) if noticeable dragging or shuffling present; zero for failure. 656 such data triplets, with same day measurement of 10m walking time, EDSS and Barthel Index assessments were available from retrospective records.

Results: Toe and heel walking scores were strongly interdependent (r²=0.69) but much less so with tandem walking (r²=0.29 and r²=0.27 respectively). 10m walking speed correlated with toe (r²=0.75), heel (r²=0.72) and tandem (r²=0.56) walking scores. Multilinear correlation analysis of 10m walking time with all three walking type scores yielded an optimal fit (r²=0.88) whose coefficients led to the construction of a Walking Disability Index (WDI) defined as: WDI = 4xTandem + 3xToe + 2xHeel. WDI correlates strongly with 10m (n=630, r²=0.86) and 6 minutes walking times (n=84, r²=0.77), but less so with EDSS (r²=0.62) and the Barthel Index (r²=0.52) scores.

Discussion: WDI definition, extended by assigning ½ to patients only able to walk aided and zero to those immobile, permits very rapid and distinctive quantitative (range zero to ten) scoring of MS patients mobility which predicts confidently the actual walking performance and may help track walking disability evolution.

P2732

Demyelinating disease following anti-TNF-α treatment. A causal or coincidental association? Report of two cases

E. Andreadou, E. Kemanetzoglou, K. Sfakianaki, M.E. Evangelopoulos, A. Rombos, E. Stamboulis

1st Department of Neurology, Athens National and Kapodistrian University, “Aeginition” Hospital, Athens, Greece

Tumour necrosis factor antagonist (anti-TNF-α) treatments are an established therapeutic option for several auto-immune and inflammatory bowel diseases. Despite their clinical effectiveness, certain neurological adverse effects have been reported in the literature. Multiple sclerosis represents a T-cell mediated auto-immune demyelinating disease of the central nervous system (CNS) induced by autoreactive pro-inflammatory T-cells. TNF is an immunomodulating cytokine implicated in the activation of autoreactive CD4 T-cells. Literature data suggest a potential role of anti-TNF-α in the induction of demyelination of the CNS. We present two patients treated with anti-TNF-α who developed symptoms suggestive of CNS demyelination. The first case is a 27-year-old male, who received etanercept for psoriatic arthritis for 8 months. The patient presented with dysethesias up to T4 level. Cervical MRI revealed an enhancing lesion (C3). The second case is a 30-year-old male treated with adalimumab for 3 years due to ankylosing spondylitis. He complained of fatigue and developed urinary urgency few months after treatment onset. He presented with right unilateral tinnitus. In both cases brain MRI showed lesions suggestive of demyelination. Anti-TNF-α treatments were discontinued and both patients showed clinical improvement after intravenous treatment with corticosteroids. Demyelination of the CNS following anti-TNF-α treatment represents a relatively rare but serious potential complication of these drugs. Close follow-up and MRI monitoring of these patients is mandatory to elucidate whether these clinical manifestations represent adverse events occurring during anti-TNF-α therapy or a first demyelinating event.
P2733

Alemtuzumab-associated infusion reactions in CARE-MS II


1Moscow City Center of Multiple Sclerosis, Moscow, Russia, 2NeuroRx Research Inc, Montreal, QC, Canada, 3Cleveland Clinic Foundation, Cleveland, OH, USA, 4University of Cambridge Medical School, Cambridge, UK, 5Universite’ Claude Bernard, Lyon, France, 6University of Texas Medical Branch, Round Rock, TX, USA, 7Heinrich-Heine University, Dusseldorf, Germany, 8Charles University in Prague, 1st Faculty of Medicine and Central Military Hospital, Prague, Czech Republic, 9Medical University, Lodz, Poland, 10Brigham & Women’s Hospital, Boston, MA, 11Advanced Neurology in Colorado, Ft. Collins, CO, 12Associates In Neurology, Lexington, KY, 13Genzyme, Cambridge, MA, USA

Objective: In CARE-MS II, the monoclonal antibody alemtuzumab was more effective than subcutaneous interferon beta-1a (SC IFNβ-1a) in reducing relapses (p<0.0001) and sustained accumulation of disability (SAD; p=0.0084) in RRMS patients who relapsed on prior therapy. We describe infusion-associated reactions (IARs) in alemtuzumab-treated patients in CARE-MS II.

Methods: CARE-MS II, a 2-year, rater-blinded trial; 840 RRMS patients who relapsed during prior therapy were randomized to alemtuzumab (12 or 24mg/day IV on 5 days at study start and 3 days 12 months later) or IFNβ-1a (44 mcg SC 3 times weekly). Methylprednisolone (1g IV) was given immediately prior to alemtuzumab for the first 3 days of the first and second courses. An IAR was defined as any adverse event (AE) during or within 24 hours after an alemtuzumab infusion.

Results: IARs were reported in 92.1% of alemtuzumab-treated patients. The most common events (experienced by 15% or more patients) were headache, rash, nausea, fever, urticaria, and pruritus. Most IARs (97.9%) were mild to moderate in severity; few were serious (2.9%). 8 patients (1.3%) discontinued study treatment due to IARs. Incidence of IARs was higher during first course compared with second (87.1% vs. 74.0%). With the exception of day 4 of course 1, which was the first day without methylprednisolone, IARs declined with each day of infusion.

Conclusions: IARs occurred frequently with alemtuzumab treatment. Most were mild to moderate, reduced with appropriate pre-treatment, and diminished with continued treatment exposure. Serious IARs generally did not preclude patients from receiving further alemtuzumab therapy.

P2734

Long-term effects of cognitive rehabilitation in multiple sclerosis: 12 months follow-up

A. Altinkaya1, I. Guclu2, E. Kurt3, A. Bingol4, D. Yandim Kuscu5, P.N. Sutlas6, D. Kirbas2, B. Topcular1,4

1Department of Neurology, Istanbul Bilim University, 2Department of Neurology, Bakırköy Teaching and Research Hospital for Mental Health and Neurological Disorders, 3Mayis Psychology Center, 4Center for Research in Emotion and Cognition, Istanbul Bilim University, Istanbul, Turkey

Objective: Cognitive impairment is a common problem in Multiple sclerosis (MS). It affects more than half of MS patients and plays a major role on quality of life, employment and social life. Studies in the recent years proved that cognitive rehabilitation is an efficient intervention for MS related cognitive impairment. However, persistency of effects of cognitive rehabilitation is undetermined.

Methods: Patients admitted to two major MS centres were randomly screened for cognitive impairment using Brief Repeatable Battery (BRB) and relapsing remitting MS patients with EDSS 1.0-5.5 reporting cognitive dysfunction were offered to participate in an 8-week trial of computer assisted cognitive rehabilitation programme. Patients were re-evaluated using BRB 3, 6 and 12 months after cognitive rehabilitation.

Results: 14 patients completed cognitive rehabilitation programme. There was a significant improvement in cognitive test scores following cognitive rehabilitation followed by a mild progressive decline in cognitive performances at 3, 6 and 12 months after cognitive rehabilitation. However, the cognitive scores in BRB were significantly better compared to baseline (before cognitive rehabilitation) even after 12 months.

Conclusions: Our results show that cognitive rehabilitation is a promising approach in treating MS related cognitive impairment. This study shows that cognitive rehabilitation is effective even 12 months after intervention although there is a decrease in cognitive performance over time. Repeated trials of cognitive rehabilitation or home-based cognitive training after rehabilitation might overcome this problem.
P2735
High-dose immunosuppressive therapy combined with autologous stem cell transplantation (HSCT) for multiple sclerosis: 10 years later
V. Rossiev¹, S.V. Makarov¹, A. Kostromina², S. Ilyichev²
¹Center of Bone Marrow and Stem Cell Transplantation, ²LDC MIBS, Samara, Russia

Introduction: Comparative evaluation of clinical and several MRI imaging data in 15 multiple sclerosis (MS) patients 10 years after HSCT therapy with cell types CD34+ as per the EBMT protocol was performed.

Subject and methods: The patient group included 9 female and 6 male patients, with age range from 18 to 51 years (Me=36) at the beginning of treatment, mean disease duration (M=9.6±5.7) years, EDSS - 6.0±0.8 points. Secondary progressive disease course was observed in 10 cases, 5 cases presented relapsing-remitting or progressive-relapsing course. High-field MRI was applied.

Results and conclusion: After HSCT therapy, the group displayed partial regression in cerebellar, improved urologic signs. In some patients, pyramidal deficit was reduced to 0.5 - 1.0. Trial status stabilization period was 6 to 96 months. In 10 years, EDSS was 6.57±0.26 (p<0.048), the signs of pyramidal deterioration (p<0.026), and cognitive impairment (p<0.003) were enhanced. Other FS scale groups of symptoms showed no statistically significant differences. Demyelization lesion burden was increased for the period only in a part of the examined group, gliosis substitution was observed. Better clinical results were noted in patients with EDSS<6.5 before HSCT, with only slight neurodegeneration signs. There is every reason to believe that HSCT slows down MS progression.

P2736
Unmatched CSF oligoclonal bands: can we differentiate between demyelinating disorders and other causes?
F. McEneaney¹, S. Kelly², J. Jackson³, M. Hutchinson³, N. Tubridy², C. McGuigan²
¹UCD School of Medicine & Medical Science, University College Dublin, ²Neurology Department, St Vincent’s University Hospital, ³Immunology Department, St James's Hospital, Dublin, Ireland

Introduction: Unmatched cerebrospinal-fluid (CSF) oligoclonal-bands (OCBs) aid diagnosis of demyelinating disorders but also occur in other inflammatory and infective conditions.

Aims: The objective of this study was to compare the profile of patients testing positive for unmatched CSF-OCBs with a diagnosis of demyelinating diseases, to those with non-demyelinating disorders.

Methods: A retrospective audit of LPs performed from January-December 2010 was completed. CSF results were examined for OCB positivity and IgG-index. Patient demographics, indication for LP and eventual diagnosis were recorded.

Results: 281 LPs were performed during the study period. Clinical indications included: suspected demyelinating disorders (44.84%) [42.70%: suspected Multiple sclerosis (MS)]; meningitis (17.79%); headache (8.19%); possible malignancy (4.98%); and idiopathic intra-cranial hypertension (4.63%). 47 (39.17%) had positive OCBs (mean age 37, mean IgG-index:1.102). Of the 47; 63.83% were eventually diagnosed with MS (63% female, mean age 37, mean IgG-index:1.114) and 19.15% with clinically-isolated syndrome (67% female, mean age 34, mean IgG-index:1.358). The remaining 17.02% had non-demyelinating conditions including: mitochondrial disorders (4.26%); encephalitis (2.13%); meningitis (2.13%); cerebral–lupus (2.13%); neuro-syphilis (2.13%); Parry-Romberg Syndrome (2.13%) and other (2%). This subgroup was primarily female (75%), with a mean age of 41 and a lower IgG index (0.769), compared to those with demyelinating disorders. Although the sample size is small, the difference in IgG index between the demyelinating and the non-demyelinating subgroups is statistically significant (p=0.0132).

Conclusion: This audit offers an interesting analysis of LPs. Subtle differences in IgG-index may aid the differentiation of demyelinating diseases from other causes of unmatched positive-OCBs in CSF.
P2737

Value of aquaporin-4 antibody in patients with neuromyelitis optica

General Hospital of Chinese PLA, Beijing, China

Objective and methods: To investigate the existence of aquaporin-4 (AQP4) antibody by indirect immunofluorescence in human AQP4-transfected cells, and to evaluate the diagnostic and prognostic value of AQP4 antibody in 210 patients with Neuromyelitis optica (NMO), High risk NMO(HR-NMO), classic multiple sclerosis (MS), and other neurological diseases.

Results: AQP4 antibody titre had statistically significant differences among patients with NMO, HR-NMO and MS (p<0.05). Meanwhile, there were statistically significant differences between the NMO/HR-NMO and MS group in terms of sex, accompanying with severe optical neuritis (ON), transverse myelitis (TM), brain MRI normal, spinal cord lesion having more than 3 segments, and AQP4 antibody positive rate (p<0.05). In addition, in 55 AQP4 seropositive patients, 36 (66.7%) were found to accompany with severe ON, 41 (75.9%) had TM, 30 (55.6%) had spinal cord lesion>3 segments, 8 (14.8%) developed ON relapse and 19 (35.2%) developed TM relapse in 24 median months follow-up study. There were statistically significant differences between antibody positive and negative patients with respect to accompanying with severe ON, TM, spinal-cord lesion>3 segments, developing ON relapse and TM relapse (p<0.05).

Conclusion: Our study suggests that AQP4 antibody is a sensitive and specific biomarker for discrimination among NMO, classical MS and other neurological diseases. It is particularly helpful to diagnose those HR-NMO patients. AQP4 antibody positive patients shows significantly higher frequencies of ON or TM relapse compared to AQP4 antibody negative patients.

P2738

Concentration of interleukins 6, 10 and TNF-α, and fatigue in patients with multiple sclerosis

E. Dworzańska, K. Mitosek-Szewczyk, Z. Stelmasiak
Neurology, Lublin Medical University, Lublin, Poland

Multiple sclerosis (MS) is a chronic inflammatory disease of the CNS with presumed auto-immune etiology. Fatigue is one of the most common disabling Symptoms. The aim of the present study was to compare serum pro-inflammatory (IL-6, TNF-α) and anti-inflammatory (IL-10) cytokine production in MS patients with and without fatigue and healthy controls. We hypothesized that fatigue would be associated with cytokine production.

Material and methods: The investigated group included 81 patients with MS and fatigue (MFIS scores ≥39, FSS scores 4.6). The first control group included 54 with MS, without fatigue (MFIS< 39, FSS scores 4.1). The second control group included 16 healthy people. Serum TNF-α and interleukins IL-6, IL-10 level were measured by ELISA assay.

Results: Mean levels of TNF-α and IL-10 were significantly higher in MS patients with fatigue than in those without fatigue. No differences were seen for IL-6

Conclusions:

1. An increase of TNF-α concentration in patients with MS is related to fatigue in these patients, which may explain the pathogenetic role of fatigue in MS developed on the immunological basis.

2. An increase in IL-10 concentration in patients with MS and fatigue may suggest the intensification of the regeneration process in response to increased activity of pro-inflammatory factors.

3. Development of fatigue in multiple sclerosis is not correlated with changes in interleukin 6 concentration, which means that participation of this pro-inflammatory cytokine in the pathogenesis of fatigue in MS is not significant.

P2739

Abstract cancelled
P2740

**Influence of subclinical hypothyroidism on neuropsychological impairment in patients with multiple sclerosis**

E. Kiseleva¹, N.N. Spirin²

¹Neurology, ²Neurology with Medical Genetics and Neurosurgery, Yaroslavl State Medical Academy, Yaroslavl, Russia

**Introduction:** Many authors have noted a higher prevalence of auto-immune thyroid disease in multiple sclerosis (MS) patients. But the influence of thyroid dysfunction on the neuropsychological status in MS patients has been studied insufficiently.

**Methods:** We examined 65 patients (17 males, 48 females) with clinical definite relapsing-remitting MS in clinical remission. The average age of patients was 36.8 years (19-61 years). Severity of neuropsychological impairments was assessed according to the Beck Depression Inventory, L.D. Malkova asthenia assessment scale, State-Trait Anxiety Inventory. All patients underwent an ultrasound examination of the thyroid gland, analysis serum thyroid hormones and antithyroid antibodies. For statistical analysis used standard statistical methods.

**Results:** In 13.8% of MS patients subclinical hypothyroidism was diagnosed, 55.5% of MS patients had different thyroid pathology without dysfunction. 30.7% of patients, who did not have thyroid disease, were the comparison group. 66% of patients with subclinical hypothyroidism were treated with IFN-β-1b, in the comparison group were only 20%.

The mean scores of asthenia, personal anxiety and depression were higher in patients with subclinical hypothyroidism, than in the comparison group - 62.5±14.08 and 51.4±17.91, 54.1±8.79 and 46.6±11.95, 22.1±17.78 and 11.4±9.81 (p<0.05).

**Conclusion:** One of the reasons of fatigue, anxiety, and depression in patients with MS may be the development of subclinical hypothyroidism. This should be considered, when planning the examination and treatment of such patients.

---

P2741

**Antibiotic therapy in patients with the combination of definite multiple sclerosis and chronic Lyme disease**

N.N. Spirin¹, O.A. Fadeeva¹, N.S. Baranova¹, E.G. Shipova¹, I.O. Stepanov²

¹Neurology, Yaroslavl State Medical Academy, ²Neurology, Clinical Hospital N°8, Yaroslavl, Russia

**Background:** In the endemic region, Lyme disease (LD) may occur among patients with definite multiple sclerosis (MS).

**Aim:** To investigate the antibiotic therapy results and clinical features in patients with definite MS and chronic LD combination.

**Methods:** Among 100 MS patients, LD was diagnosed and treated in 14 MS patients: 5 male and 9 female, mean 36.6±11.7 years old (M±σ). Sera were examined for borrelia Burgdorferi antibodies by ELISA, indirect immunofluorescence test or Western-blot.

**Results:** 8 (57.1%) patients had a tick bite (in 7 cases before the onset of MS), 1 patient had erythema migrans. Arthralgia was observed in 4 (28.6%) cases. 12 patients were treated by ceftriaxone, 1 patient by amoxicillin+clavulanic acid, 1 patient by doxycycline. Duration of antibiotic therapy was 19±6 days (M±σ). In 2 cases cerebrospinal fluid was examined by ELISA but antibodies against borrelia Burgdorferi were not detected. In all 14 cases the antibody level against borrelia Burgdorferi in serum decreased after the treatment. In 2 cases arthralgia was decreased and neurological improvement was observed in 7 (50%) patients: in 6 cases ataxia was decreased only or in combination with decrease of asthenia (3 cases), paresis (1 case), bladder dysfunction (1 case). There were no correlations between clinical improvement and the antibody level against borrelia Burgdorferi in serum or MS duration before antibiotic therapy.

**Conclusion:** The decrease of symptoms after antibiotic therapy determines the advisability of diagnosis and treatment of LD in MS patients.
P2742
Blood adipokines and their association to disability status and progression index in multiple sclerosis: a 3-year follow-up study
R. Natarajan1, M. Hämälainen2, M. Raunio1,2,4, E. Moilanen2, I. Elovaara1,3
1Dept of Neuroimmunology, Medical School, 2Immunopharmacology Research Group, Medical School, University of Tampere, 3Department of Neurology, Tampere University Hospital, 4Department of Neurology, Kanta-Häme Central Hospital, Hämeenlinna, Finland

Objectives: Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system. In the present study, we determined the 3-year follow-up levels of adipokines including leptin, adiponectin, adipisin and resistin in the sera of patients with MS and analysed their association to various clinical parameters including disease activity and progression.

Methods: The study was a 3-year prospective follow-up study that included 60 MS patients, 20 subjects with clinically isolated syndrome (CIS) and 30 healthy controls who underwent neurological examination for 3 years. Plasma adipokine levels were measured using enzyme immunoassay.

Results: At baseline and 1-year follow-up, CIS patients showed higher levels of resistin than RRMS group (p<0.05). Comparison between the CIS and CIS converted group, the baseline levels of adiponectin seemed to be increased in those subjects who converted to CDMS (p<0.01). The highest levels of adipisin were found in progressive subtypes, while in RRMS adipisin levels remained low during the entire 3-year period (p<0.05). In RRMS group, the levels of adipisin seemed to correlate positively with disability status and progression index (PI) (p<0.05). At 2-year follow-up, the levels of leptin seemed to correlate with the PI (p<0.05) in the PPMS group.

Conclusions: Our data suggest that leptin, adipisin and resistin might contribute to the development of disability and progression of the disease, while adiponectin seems to be a candidate for monitoring conversion of CIS to definite MS patients. These adipokines are important in MS pathogenesis and might be potential biomarkers.

P2743
Cortical activation changes following botulinum toxin treatment of leg spasticity in multiple sclerosis: a pilot study
J. Klosova, P. Hluštík, P. Hok, V. Sládková, J. Mareš, P. Otruba, R. Herzig, P. Kaňovský
Neurology, Faculty hospital Olomouc, Palacky University, Olomouc, Czech Republic

Background: Botulinum neurotoxin (BoNT) treatment affects multiple levels of the sensorimotor system and can relieve spasticity of lower limbs caused by multiple sclerosis. The aim of our functional magnetic resonance study was to evaluate cortical activation changes following botulinum toxin treatment of leg spasticity in multiple sclerosis.

Methodology: 4 patients (1 man, 3 women, mean age 46.5, SD 9.3 years) with multiple sclerosis affected with leg spasticity were studied. Patients performed repeated knee extension-flexion movements during brain functional MRI which was acquired in three sessions: before, 4 and 12 weeks after BoNT treatment into the spastic muscles. The change of leg spasticity was assessed using the Snow scale.

Results: BoNT treatment decreased leg spasticity across the group. FMRI pre-BoNT treatment showed extensive bilateral task-related activation of frontoparietal sensorimotor cortical areas, whereas post-BoNT treatment caused retraction to midline and contralateral sensorimotor cortex. Third examination after 12 weeks of BoNT treatment showed re-expansion to a similar extent as seen in the pre-BoNT session.

Conclusions and relevance: This pilot study suggests that relief of leg spasticity may be associated with temporary partial normalization of activation in primary and association sensorimotor cortical areas. Spasticity may be contributing to the documented compensatory over-activation of the sensorimotor system in multiple sclerosis. Supported by: Czech IGAMH grant NS9920.
P2744

Caregiver burden and self-efficacy in caregivers of multiple sclerosis patients

V. Unver¹, T. Basak¹, S. Demirkaya²
¹School of Nursing, ²Neurology, Gulhane Military Medical Academy, Ankara, Turkey

Introduction: Individual patient care is usually given at home by families in our country. Perceived as a responsibility of care giving within the family. Problems experienced by the patient do not affect just the patient. At the same time, it also affects caregivers’ family members and relatives. This study aims at examining the relationship between caregiver burden and self-efficacy in family caregivers of multiple sclerosis patients.

Methods: This study was planned and applied as a descriptive and a cross-sectional study. The study was conducted at Neurology Department of Gulhane Military Medical Academy. Data were collected by using a data collection form involving questions on the patients’ specific characteristics, Self-Efficacy Scale and Burden Interview. Permission was obtained for the study by applying to the local ethics committee. Informed consent was obtained from all participants. The application was realized by surveying on volunteer patients after making necessary explanations about the aim of the study. The survey was filled by the patients in the waiting room and took 30-45 minutes.

Results: In this research, the mean age of the family caregivers was 46.88±12.60 years. It has been stated that, of these family caregivers, 89.2% were female, 85.4% were married. Of the caregivers, average total scores for Self-Efficacy Scale were found to be 38.57±4.85. The mean of Caregiving Burden Scale scores was 23.00± 9.16. The study is still continuing.

Conclusion: The study provides important information for health care providers as they design interventions for caregiver with multiple sclerosis patients.

P2745

An anti-oxidant, paraoxonase1 activity in multiple sclerosis

L. Racz¹, J. Padra², Z. Mezei¹, G. Paragh², L. Csiba¹, I. Seres², T. Csépany²
¹Neurology, ²1st Department of Internal Medicine, University of Debrecen Medical and Health Science Center, Debrecen, Hungary

Introduction: Paraoxonase1 (PON1), an enzyme associated with high density lipoprotein (HDL), plays an important role in the anti-oxidant and anti-inflammatory properties of HDL. Increasing evidence supports a role of oxidative stress in inflammatory processes and in the pathogenesis of multiple sclerosis (MS). The aim of this study was to investigate the activity of PON1 in patients with different types of MS.

Methods: Our study involved 197 MS patients with average age of 39 years. Paraoxonase and lactonase activities of PON1 and lipid profiles were compared in subgroups of relapsing-remitting (134), benign (15), primary progressive (12), secondary progressive (19), relapsing progressive (4) and clinically isolated syndrome (13) at different stage of the disease (EDSS: group A: 0-4.0; group B: 4.5-6.5; group C: 7.0-8.0).

Results: PON1 activity did not differ in the subgroups regarding of the course of MS. PON1 activity had a tendency to be higher in patients with higher EDSS. Patients with greater disability were older and had slightly lower, but statistically not significant HDL blood levels than those of less disabled. The AA:AB phenotype ratio was approximately 1:1 among RP and benign patients and was 3:1 among RR, PP, SP and CIS patients.

Conclusion: Our results did not demonstrate association between altered lipoprotein peroxidation and different types of MS. Further studies are needed to evaluate their exact role in this disease.
P2746

Does footwear influence on gait analysis in multiple sclerosis characterization of functional ambulation and temporal spatial parameters in comparison with healthy subjects?

M. Castillo¹, A. Hochsprung²-³, G. Izquierdo⁴, B. Heredia Camacho⁴
¹Biofunctional Neurophysiotherapy Unit, Hospital Universitario Virgen de la Macarena, ²Hospital Universitario Virgen Macarena, ³Neurociencias, ⁴Neurology, Hospital Universitario Virgen Macarena, Sevilla, Spain

Background: Gait abnormalities are an early clinical symptom in MS, leading to decreased activity and limitations in function. However, how the footwear influences on and specific characterization of abnormal gait in MS patients has not been described before.

Objective: To characterize the influence footwear has on spatio-temporal gait parameters affection in MS patients and ascribe them to clinical variables, in order to compare with healthy subjects.

Methods: 30 MS patients relatively able of independent walking and 30 healthy subjects were evaluated using GAITRite, with and without footwear. Subjects also underwent a thorough neurological examination to assess their disability using the EDSS. Gait parameters are compared to characterize gait impairments in MS patients with and without footwear. The group of patients the correlation of gait parameters with clinical neurological variables was investigated. Statistical analysis two way Anova and Bonferroni post-test.

Results: MS patients demonstrated significant impairment in spatio-temporal gait parameters compared to healthy subjects and higher variation without footwear. MS patients have a lower mean FAP score; velocity and distance with significances alterations (p<0.001), cadence (p<0.05); step lengths, and single support are decreased in MS patients. FAP score negatively correlated with disease duration and EDSS.

Conclusions: Gait parameters are impaired in MS. The impaired gait patterns are correlated with the associated neurological disability. The gait without footwear significantly affected the MS patients. Specific and accurate assessment of gait without footwear can be a useful tool to monitor MS evolution and can be used to advise target oriented neurofunctional improving management. More studies are necessary.

P2747

Some features of brain dysfunctions in adolescents in cases of multiple sclerosis with or without optical neuritis

O. Yegorkina¹, N. Voloshyna¹, N. Pryvalova¹, I. Duras²
¹Institute of Neurology, Psychiatry and Narcology of the AMS of Ukraine, ²Kharkiv National Medical University, Kharkov, Ukraine

34 adolescents with verified diagnosis of multiple sclerosis (MS) according to criteria of W.McDonald et al. (2010), 26 of them with acute neuritis of optical nervus (ON) and 8 without ON, were studied with optical coherent tomography, visual evoked potentials (VEP), and MRI. The results of research allowed finding correlations between such parameters as decrease of middle thickness of retina nervous fibres layer, loss of vision fields, impairments of VEP manifested as increase of basic cortical potential latency and diminution of response amplitude. All of these disorders were more expressed in patients suffering from MS with ON. The data of neuropsychological examination by Luria’s method have shown that in a case of MS with ON the main disorders of higher mental functions included impairments of object image recognition in complicated conditions of perception, mild disorders of spatial praxis and visual space perception, simultaneous discrimination, memorizing of spatial configuration of visual stimuli side by side with signs of semantic aphasias, disturbances of understanding of numerous constructions and calculations with crossing ten. The data obtained may testify dysfunction of brain system which not only realizes visual functions on all levels of organization, but also provides processing of relevant information with using complex symbolic codes. Data of MRI have shown that the impairments found may be conditioned by lesion of thalamic non-specific system realizing visual attention by conducting of relevant sensory stimuli while lesions of peripheral parts of visual analyzer, pathways, projective and associative visual areas are not significant.
P2748
Progression of cognitive indicators and quality of life in multiple sclerosis
N. Drazhina
BSMU, Minsk, Belarus

**Background:** The influence of autologous mesenchymal stem cells transplantation (AMSCT) on the brain’s integrative functions changing and life quality improving in patients with multiple sclerosis (MS) is of great interest.

**Objective:** To assess the changes of cognitive indicators and quality of life in MS patients after AMSCT.

**Methods:** 56 patients (26 in the main group, 30 in the control group) were included in the study. The diagnosis was verified by the McDonald and al. (2005y.) criteria. Cognitive indicators were followed during 2 years after AMSCT with Short Cognitive Performance Test (SKT), Paced Auditory Serial Addition Test (PASAT). The quality of life was investigated by SF-36. Fatigue was assessed on the FIS scale.

**Results:** After AMSCT the positive dynamics of decreasing of fatigue was registered in 58.1% of patients. The initial indicators on SKT scale were 14.2±1.8 in main group, 14.3±1.7 - in control one. After the follow-up decreasing of these indicators by 3.2 ±1.1 was registered in main group, and only by 0.3 (±1.2) in control group. Physical component after treating was 198.44±48.54 in main group and 134.45±21.12 in control one. The psychological component of quality of life was 228±34.83 in main group and in control one - 120±63.24 (p<0.05). The tendency of significant improvement of psychological component was noted, first of all VT, MH, RE ( p< 0.05).

**Conclusions:** AMSCT improves the psychomotor activity and cognitive functions. The observed changes of cognitive indicators may be modified after AMSCT, and it can improve the quality of life of patients with MS.

P2749
Speed of recovery in walking after multiple sclerosis relapses
K. Kannel1, H. Maamägi1, K. Taalfeld1, M. Toots1, M. Siirõ1, K. Kallaste1, L. Vahter1,2, T. Saarup1,2, K. Rohulaid1,2, I. Zopp1, S. Pajuste1, A. Aaso1, U. Sorro1, K. Gross- Paju1,3
1Estonian MS Centre, West- Tallinn Central Hospital, 2Institute of Psychology, Tallinn University, 3Institute of Clinical Medicine, Tallinn University of Technology, Tallinn, Estonia

**Introduction:** Reduced walking ability is common during multiple sclerosis (MS) relapses. 17% change in walking speed is clinically important. When to define non-responders to adequate course of methylprednisolone for relapses is unclear. The definition of failed first line relapse treatment helps to administer higher doses of glucocorticoids or plasmapheresis in timely manner.

**Goals:** Examination of walking ability and speed of recovery in MS relapses.

**Methods:** 31 persons with multiple sclerosis (PwMS) were recruited from April 2010. 4 patients had 2 relapses during the study, so 35 relapses were assessed. PwMS were evaluated with Disability Status Scale (EDSS), 6 Minute Walk Test (6MWT), Multiple Sclerosis Walking Scale (MSWS). Relapses were treated with 5g of intravenous methylprednisolone (IVMP). Walking was assessed during relapse, after the first and the last IVMP drip, 1 month and 3 months after relapse.

**Results:** Statistically and clinically important improvement was demonstrated comparing MSWS during relapse and after 5th IVMP drip 20% (p≤0.0001), which remained unchanged later. Moderate but statistically significant improvement was shown comparing EDSS during relapse vs. 1 month (p=0.0001) and 3 months (p=0.0076) after relapse. There was also improvement comparing 6MWT during relapse and after 1st IVMP drip 5.7% (p≤0.0001), that remained stable later.

**Conclusions:** Statistically significant improvement after IVMP relapse treatment was demonstrated with all walking-based outcome measures. Only MSWS change was clinically important, which was evident already after 5th IVMP drip and remained stable thereafter. Results suggest effectiveness of IVMP therapy and indication for second treatment regimen can be determined early.
P2750

Analysis of the efficiency of combining disease-modifying treatment and phytotherapy in patients with relapsing-remitting multiple sclerosis

O.D. Barnaulov¹, T.V. Osipova²
¹The Bektireva Human Brain Institute, RAS, ²I.P.Pavlov State Medical University, Saint Petersburg, Russia

Aim: To explore clinical characteristics of disease progression in patient with multiple sclerosis (MS) treated with combination of disease-modifying treatment and polycomponent phytotherapeutic treatment.

Methods: In this study 74 patients were separated in two groups, of which A-group was treated with disease-modifying treatments (DMT) and the other - B-group, had polycomponent phytotherapeutic treatment in addition to DMT. The A-group consists of 36 patients, the B-group consists of 38 patients. The expanded disability status scale (EDSS), transformation of relapsing-remitting (RR) MS in secondary progressive (SP) MS and annual replace rate (ARR) was compared in this study.

Results: Median time to EDSS 3 in 39% of patients was 2.8 years (A-group) versus 9 years in 2.6% cases (B-group). Median time to EDSS 4 in 33% patients was 1.8 years (A-group) and 2 years in 5.3% cases (B-group). Median time to EDSS 6 in 13.9% cases was 3 years (A-group), 10.5% - 3.8 years (B-group). Transformation to SPMS: in 25% cases (A-group), 10.5% cases (B-group). ARR in A-group was 0.8 relapses per year, which was 1.3 before treatment. ARR in B-group was 0.16 relapses per year with baseline ARR - 1.1.

Conclusion: Patients with combination of DTM and phytotherapy had a longer period to reach disability - EDSS 3, 4 (p<0.01), SDSS 6 and transformation in SPMS (p<0.05) then patients with DTM only. These results may show the need of larger findings in phytotherapeutic multiple sclerosis treatment research.

P2751

Antibodies against EBV, CMV, VZV, HSV-1, HSV-2, HHV-6B and borrelia Burgdorferi and viral nucleic acids in serum and CSF samples of patients with multiple sclerosis

T. Tetik Kosan¹, H. Mavioglu², T. Sanlidag³, S. Akcali³, T. Ecemis³, G. Dinc Horasan⁴
¹Neurology, Yozgat Devlet Hastanesi, Yozgat, ²Neurology, ³Microbiology, ⁴Biostatistic, Celal Bayar University, Manisa, Turkey

Introduction: The main objective of this study is investigating antibodies against human herpes virus and spirochaete borrelia Burgdorferi, having high potential to play a role in the etiology of MS, and viral nucleic acids of these agents in the samples of serum and CSF of patients with MS.

Methods: VCA IgG, EBNA IgG, EA IgG for EBV, CMV IgG, VZV IgG, HSV1 IgG, HSV2 IgG, HHV6B IgG and Borrelia Burgdorferi IgM/IgG antibodies were studied by ELISA and viral nucleic acids by PCR in the serum of MS patients (n=44) and patients with other inflammatory neurological disease (control-1) (n=23), and subjects without any organic neurological disease (control-2) (n=23). In addition, nucleic acids of these agents were investigated by PCR in the CSF samples of some cases from MS group (n=17) and control-1 group (n=20).

Results: Comparing rates of EBV, CMV, VZV, HSV-1, HSV-2 and borrelia Burgdorferi antibody positivity in the serum samples of patients with MS and control groups, there was no significant difference between groups. However, rates of HHV-6B antibody positivity in patients with MS were significantly lower comparing with control-1 and control-2 groups, being 68.2%, 91.3% and 95.7%, respectively. According to nucleic acid of agents, only HHV-6B were found in one MS patient’s serum and in one control-1 patient’s CSF.

Conclusion: In this study, only HHV-6B IgG positivity in serum samples of MS patients was found significantly lower compared with control subjects. It may be coincidental or may show an unknown relationship.
P2752

The effect of natalizumab therapy on executive function, fatigue and depression in patients with multiple sclerosis

S. Jónsdóttir1,2, H. Hjaltason1,2, S. Bráínsdóttir1,2
1Neurology, Landspitali-The National University Hospital of Iceland, 2Faculty of Medicine-School of Health Sciences, University of Iceland, Reykjavík, Iceland

Objective: The objective of this study was to examine if one-year therapy with natalizumab has an effect on executive function, fatigue and depressive symptoms in patients with relapsing-remitting multiple sclerosis.

Method: 40 MS patients (mean age 41.7 years; 23 females, 17 males; mean education 15.2 years) who received natalizumab therapy at the National University Hospital of Iceland 2008 to 2011 participated in the study. Just before therapy started patients and informants (usually spouses) completed measures assessing executive function (Behaviour Rating Inventory of Executive Function-Adult Version, BRIEF-A). In addition questionnaires measuring fatigue (Modified Fatigue Impact Scale, MFIS) and depression (Beck Depression Inventory-II, BDI-II) were administered. The MFIS was also administered to 20 healthy controls with one year interval. Differences from baseline were evaluated using the Wilcoxon test and p<0.05 was considered statistically significant.

Results: Significant improvement was observed on executive function both according to patients themselves (Global Executive Composite, GEC, p=0.01) and informants (GEC, p=0.01). Scales measuring cognitive control (Metacognition Index, MI), improved but not those measuring behavioural control (Behavioural Regulation Index, BRI) both according to patients (MI, p=0.00; BRI, p=0.32) and informants (MI, p=0.01; BRI, p=0.07). Fatigue declined significantly in patients (p=0.00) while it remained unchanged in controls (p=1.00). Symptoms of depression also declined significantly in patients (p=0.00).

Conclusion: After one year of therapy with natalizumab executive function had significantly improved both according to MS patients themselves and informants. Both fatigue and depressive symptoms declined significantly.

P2753

Association of PPAR γ Pro12Ala polymorphism with susceptibility to and severity of MS in Iranian people

A. Rahimi Jaberi, G. Yoosefipour, E. Kamali Sarvestani, M. Sharifian Dorche
Shiraz University of Medical Sciences, Shiraz, Iran

Introduction: Multiple sclerosis (MS) is a progressive auto-immune neurodegenerative disorder of the CNS that is characterized with inflammation and demyelination of the CNS, which culminates in neurological deficits and paralysis. Numerous studies have revealed that agonists of peroxisome proliferators-activated receptor-gamma (PPAR γ) exert anti-inflammatory effects both in vitro and in vivo and may play a role in MS.

Method: We examined the association of PPAR γ Pro12Ala polymorphism with susceptibility to and severity of MS in Iranian people.

Results: In a case-control analysis that included 254 multiple sclerosis cases and 217 matched controls, we found significant difference in distribution of this polymorphism between patients and controls (P value=0.029) but not significant association between sex (in female group P value=0.816, in male group P value=0.722), disease type (P value=0.690). And disability index (EDSS) (P value=0.943) progress index (EDSS/duration) (P value=0.943) disease onset age (P value=0.486).

Discussion: We conclude that the Pro12Ala polymorphism does appear to play a significant role in susceptibility to MS in this study.
P2754
Comparison of self-destructive personality tendencies in MS patients and healthy subjects
S. Tahbaz¹, S.M. Nabavi², N. Ghorbani³
¹Tehran University, ²Neurology, Shahed University, Tehran, Iran

P2757
Initial MR imaging and the risk of developing multiple sclerosis in patients presented with clinically isolated syndrome
Department of Neurology, Hallym University College of Medicine, Seoul, Republic of Korea

P2758
Neuromyelitis optica: a case report of a 34-year-old Slovak patient with the verified presence of antibodies against aquaporin-4 in serum and CSF
P. Koson¹,², P. Spalek¹, I. Martinka¹, F. Jurcaga¹, A. Berthele³, S. Mader⁴
¹Department of Neurology of Slovak Medical University, University Hospital Bratislava, Nemocnica Ruzinov, ²Institute of Neuroimmunology, Slovak Academy of Sciences, Bratislava, Slovak Republic, ³Neurologische Klinik und Poliklinik, Technische Universität München, Munich, Germany, ⁴Abteilung für Neurobiologie, Universitätsklinik für Neurologie, Medizinische Universität Innsbruck, Innsbruck, Austria